```
=> file biosis caba caplus lifesci medline
=> e momotani e/au
E1
               MOMOTANDI EIKI/AU
E2
            1
                 MOMOTANI A/AU
E3
          167 --> MOMOTANI E/AU
E4
           3 MOMOTANI EI ICHI/AU
E5
           65
                MOMOTANI EIICHI/AU
           2
E6
                MOMOTANI EIJI/AU
E7
           8
                MOMOTANI EIKI/AU
E8
          27
                MOMOTANI H/AU
E9
          38
                MOMOTANI HIROSHI/AU
E10
          4
                MOMOTANI HISAKO/AU
E11
           1 MOMOTANI JUNICHI/AU
2 MOMOTANI K/AU
E12
=> s e3-e7 and mycobact?
           52 ("MOMOTANI E"/AU OR "MOMOTANI EI ICHI"/AU OR "MOMOTANI EIICHI"/A
              U OR "MOMOTANI EIJI"/AU OR "MOMOTANI EIKI"/AU) AND MYCOBACT?
=> dup rem 11
PROCESSING COMPLETED FOR L1
L2
            20 DUP REM L1 (32 DUPLICATES REMOVED)
=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 20 ANSWERS - CONTINUE? Y/(N):v
    ANSWER 1 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
    2007:428046 CAPLUS <<LOGINID::20080325>>
AN
    146:416306
DN
TT
   Primer sets for detection of expression level of urocortin for evaluation
    of progressing of johne's disease in livestock
      ***Momotani, Eiichi*** ; Mori, Yasuyuki; Wang, Hong Yu
TN
PA National Agriculture Bio-Oriented Research Organization, Japan
SO Jpn. Kokai Tokkyo Koho, 15pp.
    CODEN: JKXXAF
DT Patent
LA
    Japanese
FAN.CNT 1
    PATENT NO.
                     KIND DATE
                                       APPLICATION NO.
                                                             DATE
                      ----
   JP 2007097490
                            20070419
                                        JP 2005-291868
                       A
PRAI JP 2005-291868
                             20051005
    This invention provides primer sets for detection of expression level of
```

urocortin in livestock blood sample by realtime-PCR. The cDNA sequence of Bos taurus urocortin were disclosed. The invention also provides method for prepn. of std. curve for real-time PCR by detecting the expression level of urocortin gene in Bos taurus cells immunized with antigen from \*\*\*Mycobacterium\*\*\* paratuberculosis. The method provided in this

invention can be used for evaluation of progressing of johne's disease in livestock in early stage of infection.

IN \*\*\*Momotani, Eiichi\*\*\* ; Mori, Yasuyuki; Wang, Hong Yu

AB . . . curve for real-time PCR by detecting the expression level of urocortin gene in Bos taurus cells immunized with antigen from \*\*\*Mycobacterium\*\*\* paratuberculosis. The method provided in this

invention can be used for evaluation of progressing of johne's disease in livestock in. . .

\*\*\*Mycobacterium\*\*\* avium paratuberculosis TT

(infection of; primer sets for detection of expression level of urocortin for evaluation of progressing of johne's disease in livestock)

- L2 ANSWER 2 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 1
- AN 2007:589654 BIOSIS <<LOGINID::20080325>>
- DN PREV200700590889
- TI Corticotropin-releasing hormone and urocortin expression in peripheral blood cells from experimentally infected cattle with \*\*\*Mycobacterium\*\*\* avium subsp paratuberculosis.
- AU Wang, Hongyu; Aodon-geril; Shu, Yujing; Momotani, Yuriko; Wang, Xiaofei; Mori, Yasuyuki; \*\*\*Momotani, Eiichi\*\*\* [Reprint Author]
- S Natl Inst Anim Hlth, Res Team Paratuberculosis, 3-1-5 Kan-nondai, Tsukuba, Ibaraki 3050856, Japan momoteni@affrc.go.jp
- SO Microbes and Infection, (JUL 2007) Vol. 9, No. 9, pp. 1061-1069. ISSN: 1286-4579.
- DT Article

AB

- LA English
- ED Entered STN: 21 Nov 2007
- Last Updated on STN: 21 Nov 2007
- hormone (CRH) family which plays an important role in immune responses.

  \*\*\*Mycobacterium\*\*\* avium subspecies paratuberculosis (Map) is the
  etiological agent of paratuberculosis (Johne's disease). The role of UCN
  or CRH in the pathogenesis of Map-infection is unknown. In the present
  study, we first cloned the bovine UCN gene and demonstrated the profile of
  UCN or CRH avyression in peripheral blood calls from Map-infected cattle

Urocortin (UCN) is a new neuropeptide of the corticotrophin-releasing

- UCN or CRH expression in peripheral blood cells from Map-infected cattle and uninfected controls by real-time reverse transcription-polymerase chain reaction (RT-PCR) and BLISA analysis. These data are the first observations of the characteristic kinetics of these neuropeptides in Map-infection. UCN or CRH expression in non-stimulated blood samples from infected cattle was higher than that in similarly treated samples from uninfected controls, however, exposure to Map lysate and live Map resulted in down-regulated expression of UCN in infected cattle compared to their counterparts from uninfected controls. These results have provided a direction in understanding the pathogenesis of paratuberculosis and improving diagnostic methods for Map-infection. (C) 2007 Blesvier Masson
- TI Corticotropin-releasing hormone and urocortin expression in peripheral blood cells from experimentally infected cattle with \*\*\*Mycobacterium\*\*\* avium subsp paratuberculosis.
- AU Wang, Hongyu; Aodon-geril; Shu, Yujing; Momotani, Yuriko; Wang, Xiaofei; Mori, Yasuyuki; \*\*\*Momotani, Eiichi\*\*\* [Reprint Author]
- AB. . . Urocortin (UCN) is a new neuropeptide of the corticotrophinreleasing hormone (CRH) family which plays an important role in immune responses. \*\*\*Mycobacterium\*\*\* avium subspecies paratuberculosis (Map) is the etiological agent of paratuberculosis (Johne's disease). The role of UCN or CRH in the. . .
- Chordata; Animalia
  - Organism Name
    - bovine (common): host

SAS. All rights reserved.

- Taxa Notes
  - Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

```
***Mycobacteriaceae*** 08881
    Super Taxa
           ***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria: Bacteria: Microorganisms
    Organism Name
           ***Mycobacterium*** avium paratuberculosis (subspecies): pathogen
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
T. 2
    ANSWER 3 OF 20 CABA COPYRIGHT 2008 CABI on STN
    2008:43487 CABA <<LOGINID::20080325>>
AN
DN
    20083029329
    Molecular strategies for studying hosts of Johne's disease
TΙ
      ***mycobacterium***
      ***Momotani, E.*** ; Aodongeril; Momotani, Y.
AIT
SO.
    Journal of Veterinary Medicine, Japan, (2007) Vol. 60, No. 10, pp.
    807-813. 41 ref.
    Publisher: Buneido Publishing Company Ltd. Tokvo
    ISSN: 0447-0192
    URL: http://www.buneido-svuppan.com
CY
   Japan
DT
   Journal
LA.
   Japanese
   Entered STN: 7 Feb 2008
    Last Updated on STN: 7 Feb 2008
    Molecular strategies for studying hosts of Johne's disease
      ***mvcobacterium***
ΑU
      ***Momotani, E.*** ; Aodongeril; Momotani, Y.
вт
      ***Mycobacterium*** avium; ***Mycobacterium*** ;
      ***Mycobacteriaceae*** ; Firmicutes; bacteria; prokaryotes
ORGN ***Mycobacterium*** avium subsp. paratuberculosis
    ANSWER 4 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
L2
AN
    DN
    142:334896
   Method for diagnosing johne's disease
      ***Momotani, Eiichi*** ; Mori, Yasuyuki; Hikono, Hirokazu; Buza, Joram
    Josephat
PA
    Incorporated Administrative Agency National Agriculture and Bio-Oriented
    Research Organization, Japan
SO
   PCT Int. Appl., 38 pp.
    CODEN: PIXXD2
DT
    Patent
T.A
    Japanese
FAN.CNT 1
                     KIND DATE
                                       APPLICATION NO. DATE
    PATENT NO.
                       ____
    WO 2005029079
                       A1 20050331 WO 2003-JP11845
                                                              20030917
        W: AU, JP, US
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
           IT, LU, MC, NL, PT, RO, SE, SI, SK, TR
    AU 2003272880 A1 20050411 AU 2003-272880
                                                              20030917
    US 2008038758
                       A1
                            20080214 US 2007-572514
                                                              20070426
PRAI WO 2003-JP11845 A
                             20030917
AB A method for diagnosing johne's disease is provided, with which an animal
    infected with ***Mycobacterium*** paratuberculosis (Johne's) can be
```

ORGN Classifier

diagnosed at a high sensitivity in the inapparent infection stage before the specific antibody level begins to increase, and a large no. of specimens can be treated. The method is characterized in that it comprises collecting a blood sample of a subject animal, adding an anti-IL-10 antibody and a "\*\*Mycobacterium\*\*\* paratuberculosis antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma. yield in the cultured blood. The method is also characterized in that the IFN.gamma. yield in blood is measured by the IFN.gamma. ELISA method. Also provided is a method for diagnosing "\*\*"mycobacteriosis\*\*\*, which is characterized by comprising collecting a blood sample of a subject animal, adding an anti-IL-10 antibody and a "\*\*Mycobacterium\*\*\* antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma. yield in the cultured blood.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

- IN \*\*\*Momotani, Eiichi\*\*\* ; Mori, Yasuyuki; Hikono, Hirokazu; Buza, Joram Josephat
- AB A method for diagnosing johne's disease is provided, with which an animal infected with \*\*\*Mycobacterium\*\*\* paratuberculosis (Johne's) can be diagnosed at a high sensitivity in the inapparent infection stage before the specific antibody level begins. . . is characterized in that it comprises collecting a blood sample of a subject animal, adding an anti-II-10 antibody and a \*\*\*Mycobacterium\*\*\* paratuberculosis antige to the collected blood followed by culturing, and then, measuring the IFN.gamma. yield in the cultured blood. The . . that the IFN.gamma yield in blood is measured by the IFN.gamma ELISA method. Also provided is a method for diagnosing \*\*\*mycobacterius\*\*\* , which is characterized by comprising collecting a blood sample of a subject animal, adding an anti-II-10 antibody and a \*\*\*Mycobacterium\*\*\* antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma. yield in the cultured blood.

IT Animals

Blood analysis

Diagnosis

\*\*\*Mycobacterium\*\*\* avium paratuberculosis (method for diagnosing johne's disease by measuring blood IFN.gamma. by ELISA)

- L2 ANSWER 5 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 2
- AN 2004:438665 BIOSIS <<LOGINID::20080325>>
- DN PREV200400437489
- TI Neutralization of interleukin-10 significantly enhances gamma interferon expression in peripheral blood by stimulation with Johnin purified protein derivative and by infection with \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in experimentally infected cattle with paratuberculosis.
- AU Buza, Jorann J.; Hikono, Hirokazu; Mori, Yasuyuki; Nagata, Reiko; Hirayama, Sachiyo; Bari, Abusaleh M.; Aodon-geril; Shu, Yujing; Tsuji, Noriko M.; \*\*\*Momotani, Elichi\*\*\* [Reprint Author]
- CS ParaTB and Inflammatory Bowel Dis Res Team, NIAH, 3-1-5 Kannondai, Tsukuba, Ibaraki, 3050856, Japan momotani@affrc.go.jp
- SO Infection and Immunity, (April 2004) Vol. 72, No. 4, pp. 2425-2428. print. ISSN: 0019-9567 (ISSN print).
- DT Article
- LA English
- ED Entered STN: 17 Nov 2004

```
Last Updated on STN: 17 Nov 2004
    Monoclonal antibody neutralization of interleukin-10 (IL-10) increased
    Johnin purified protein derivative-induced whole-blood gamma interferon
    (IFN-gamma) secretion 23-fold and also increased IFN-gamma secretion
    ninefold following in vitro ***Mycobacterium*** avium subsp.
    paratuberculosis infection of peripheral blood mononuclear cells. These
    results demonstrate the suppressive effect of IL-10 on immune responses to
    M. avium subsp. paratuberculosis infection in cattle.
    . . interleukin-10 significantly enhances gamma interferon expression in
    peripheral blood by stimulation with Johnin purified protein derivative
    and by infection with ***Mycobacterium*** avium subsp.
    paratuberculosis in experimentally infected cattle with paratuberculosis.
    . . Buza, Jorarn J.; Hikono, Hirokazu; Mori, Yasuyuki; Nagata, Reiko;
    Hirayama, Sachiyo; Bari, Abusaleh M.; Aodon-geril; Shu, Yujing; Tsuji,
    Noriko M.; ***Momotani, Eiichi*** [Reprint Author]
    . . increased Johnin purified protein derivative-induced whole-blood
    gamma interferon (IFN-gamma) secretion 23-fold and also increased
    IFN-gamma secretion ninefold following in vitro ***Mycobacterium***
    avium subsp. paratuberculosis infection of peripheral blood mononuclear
    cells. These results demonstrate the suppressive effect of IL-10 on
    immune responses. . .
ORGN . . .
       Animalia
    Organism Name
       cattle (common): immune responses
       Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,
       Nonhuman Mammals, Vertebrates
ORGN Classifier
           ***Mvcobacteriaceae***
                                     08881
    Super Taxa
            ***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria; Bacteria; Microorganisms
    Organism Name
           ***Mycobacterium*** avium paratuberculosis (subspecies)
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
1.2
    ANSWER 6 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN
    2004:885718 CAPLUS <<LOGINID::20080325>>
DN
    141:363746
TI
    Development of early-stage diagnostic method for Johne disease by using
    anti-IL-10 antibody
AII
      ***Momotani, Eiichi*** ; Mori, Yasuyuki
CS
    Natl. Agric. Bio-oriented Res. Org., Natl. Inst. Animal Health, Tsukuba,
    305-0856, Japan
SO
    BRAIN Techno News (2004), 105, 18-24
    CODEN: BTEEEC; ISSN: 1345-5958
PB
    Nogyo, Seibutsukei Tokutei Sangyo Gijutsu Kenkyu Kiko, Seibutsukei Tokutei
    Sangyo Gijutsu Kenkyu Shien Senta
    Journal; General Review
LA
    Japanese
AB
    A review on early-stage diagnosis of Johne's disease (paratuberculosis) in
```

cattle by modified interferon .gamma. ELISA assay using IL-10 neutralizing

antibody, and its effectiveness.

\*\*\*Momotani, Eiichi\*\*\* ; Mori, Yasuyuki

AU

тт

Bos taurus

- \*\*\*Mycobacterium\*\*\* avium paratuberculosis (early-stage diagnosis method for Johne's disease using anti-IL-10 antibody)
- L2 ANSWER 7 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on SIN DUPLICATE 3
- AN 2004:64047 BIOSIS <<LOGINID::20080325>>
- DN PREV200400065534
- TI \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis infection causes suppression of RANTES, monocyte chemoattractant protein 1, and tumor necrosis factor alpha expression in peripheral blood of experimentally infected cattle.
- AU Buza, Joram J.; Mori, Yasuyuki; Bari, Abusaleh M.; Hikono, Hirokazu; Aodon-geril; Hirayama, Sachiyo; Shu, Yujing; \*\*\*Momotani, Eiichi\*\*\* [Report Author]
- CS Paratuberculosis and Inflammatory Bowel Disease Research Team, NIAH, 3-1-5 Kan-nondai, Tsukuba, 305-0856, Japan momotani@affrc.qo.jp
- SO Infection and Immunity, (December 2003) Vol. 71, No. 12, pp. 7223-7227. print.
  ISSN: 0019-9567 (ISSN print).
- DT Article
- LA English
- ED Entered STN: 28 Jan 2004
  - Last Updated on STN: 28 Jan 2004
- AB Blood from cattle with subclinical \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis infection was stimulated with M. avium subsp. paratuberculosis antigens, and expression of interleukin-lbeta (IL-lbeta), tumor necrosis factor alpha (INF-alpha), RANTES, monocyte chemoattractant protein 1 (MCP-1), and IL-8 was measured. Expression of ThF-alpha, RANTES, and MCP-1 was lower in infected than in uninfected cattle. The reduced response may weaken protective immunity and perpetuate infection.
- AU Buza, Joram J.; Mori, Yasuyuki; Bari, Abusaleh M.; Hikono, Hirokazu; Aodon-geril; Hirayama, Sachiyo; Shu, Yujing; \*\*\*Momotani, Eiichi\*\*\* [Reprint Author]
- AB Blood from cattle with subclinical \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis infection was stimulated with M. avium subsp. paratuberculosis antigens, and expression of interleukin-lbeta (IL-lbeta), tumor necrosis factor.
- ORGN . . . Animalia
  - Organism Name
    - cattle (common): host, breed-Holstein
  - Taxa Notes
  - Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
- ORGN Classifier
  - \*\*\*Mycobacteriaceae\*\*\* 08881
  - Super Taxa
    - \*\*\*Mycobacteria\*\*\* ; Actinomycetes and Related Organisms; Eubacteria: Bacteria: Microorganisms
  - Organism Name
  - \*\*\*Mycobacterium\*\*\* avium paratuberculosis (subspecies): pathogen Taxa Notes

## Bacteria, Eubacteria, Microorganisms

- ANSWER 8 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2003:399194 CAPLUS <<LOGINID::20080325>>
- DN 140:39839
- TT Studies on diagnostic methods for bovine paratuberculosis
- ΑU Mori, Yasuyuki; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Hikono, Hirokazu; \*\*\*Momotani, Eiichi\*\*\*
- Immune System Section, Department of Immunology, National Institute of CS Animal Health, Tsukuba, 305-0856, Japan
- SO Dobutsu Eisei Kenkyusho Kenkyu Hokoku (2003), Volume Date 2002, 109, 33-42 CODEN: DEKKC9; ISSN: 1347-2542
- PB Nogyo Gijutsu Kenkyu Kiko Dobutsu Eisei Kenkyusho
- DT Journal
- LA Japanese

AB

- Current diagnostic tests for paratuberculosis principally rest on serol. assay, bacterial culture and the johnin skin test. However, diagnostic tests that are both sensitive and specific for detecting all subclinically affected animals have not vet been found. Therefore, a no. of studies have been conducted in order to find rapid and accurate diagnostic methods for paratuberculosis. As a result, the following have been found. (1) PCR test with internal control DNA is accurate, sensitive and rapid for the detection of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in fecal samples. (2) In the interferon gamma (IFN-.gamma.) assay using johnin purified protein deriv. (J-PPD), bovine tuberculin PPD and Con A (Con A), IFN-.gamma. responses against J-PPD were the highest in affected animals. On the contrary those of Con A were the highest in healthy animals. Interpretation of the IFN-.gamma. assay by the higher IFN-.gamma. responses against J-PPD than those of Con A is preferable as one of the diagnostic criteria. (3) Monoclonal antibody (711-1-1) which recognizes the lipoarabinomannan antigen of M. avium subsp. paratuberculosis did not react with M. avium subsp. avium, and showed potential usefulness in the serol. tests. (4) A recombinant alkyl hydroperoxide reductase C of M. avium subsp. paratuberculosis has been prepd. and successfully applied to induce IFN-.gamma. from peripheral blood mononuclear cells of animals infected with M. avium subsp. paratuberculosis. (5) In the course of study on the role of cytokines, monocyte chemoattractant protein-1 seems to be involved in the pathogenesis of paratuberculosis.
- AU Mori, Yasuyuki; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Hikono, Hirokazu; \*\*\*Momotani, Eiichi\*\*\*
- AB . . . following have been found. (1) PCR test with internal control DNA is accurate, sensitive and rapid for the detection of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in fecal samples.
- (2) In the interferon gamma (IFN-.gamma.) assay using johnin purified protein
- deriv. (J-PPD), bovine. . cattle \*\*\*Mvcobacterium\*\*\* paratuberculosis infection surface antigen IFN induction test; alkyl hydroperoxide reductase antigen cattle IFN induction \*\*\*Mycobacterium\*\*\* ; reverse transcription PCR monocyte chemoattractant protein mRNA assay
- ΙT Bos taurus
  - Infection
    - \*\*\*Mycobacterium\*\*\* avium paratuberculosis (studies on diagnostic methods for bovine paratuberculosis)
- L2 ANSWER 9 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

DUPLICATE 4

- AN 2003:329566 BIOSIS <<LOGINID::20080325>>
- DN PREV200300329566
- TI Studies on the diagnostic methods for bovine paratuberculosis.
- AU Mori, Yasuyuki [Reprint Author]; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Hikono, Hirokazu; \*\*\*Momotani, Eiichi\*\*\*
- CS Immune System Section, Department of Immunology, National Institute of Animal Health, 3-1-5 Kannondai, Tsukuba, Ibaraki, 305-0856, Japan yamori@affrc.go.jp
- SO Bulletin of the National Institute of Animal Health, (2002) No. 109, pp. 33-42. print.
- ISSN: 1347-2542 (ISSN print). DT Article
- LA Japanese
- ED Entered STN: 16 Jul 2003
- Last Updated on STN: 16 Jul 2003
- Last Updated on SIN: 16 Jul 2003
  - Current diagnostic tests for paratuberculosis principally rest on serological assay, bacterial culture and the johnin skin test. However, diagnostic tests that are both sensitive and specific for detecting all subclinically affected animals have not yet been found. Therefore, a number of studies have been conducted in order to find rapid and accurate diagnostic methods for paratuberculosis. As a result, the following have been found; 1) PCR test with internal control DNA is accurate, sensitive and rapid for the detection of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in faecal samples. 2) In the interferon gamma (IFN-gamma) assay using johnin purified protein derivative (J-PPD), bovine tuberculin PPD and concanavalin A (Con A), IFN-gamma responses against J-PPD were the highest in affected animals. On the contrary those of Con A were the highest in healthy animals. Interpretation of the IFN-gamma assay by the higher IFN-gamma responses against J-PPD than those of Con A is preferable as one of the diagnostic criteria. 3) Monoclonal antibody (711-1-1) which recognizes the lipoarabinomannan antigen of M. avium subsp. paratuberculosis did not react with M. avium subsp. avium, and showed potential usefulness in the serological tests. 4) A recombinant alkyl hydroperoxide reductase C of M. avium subsp. paratuberculosis has been prepared and successfully applied to induce IFN-gamma from peripheral blood mononuclear cells of animals infected with M. avium subsp. paratuberculosis. 5) In the course of study on the role of cytokines, monocyte chemoattractant protein-1 seems to be involved in the pathogenesis of paratuberculosis.
- AU Mori, Yasuyuki [Reprint Author]; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Hikono, Hirokazu; \*\*\*Momotani, Eiichi\*\*\*
- AB. . . following have been found; 1) PCR test with internal control DNA is accurate, sensitive and rapid for the detection of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in faecal samples. 2) In the interferon gamma (IFN-gamma) assay using johnin purified protein derivative (J-PPD), bovine. . .

ORGN . .

Chordata; Animalia

Organism Name

bovine (common): host

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

ORGN Classifier

\*\*\*Mycobacteriaceae\*\*\* 08881

Super Taxa

```
***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria; Bacteria; Microorganisms
    Organism Name
           ***Mycobacterium*** avium paratuberculosis (subspecies): pathogen,
       strain-ATCC 19698, strain-Kag-1
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
    ANSWER 10 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
L2
AN
    2000:469951 BIOSIS <<LOGINID::20080325>>
DN
    PREV200000469951
    Adhesion molecules and chemokines in granulomas by ***Mycobacterium***
    avium subspecies paratuberculosis in TNF alpha deficient mice.
AU
      ***Momotani, E.*** ; Miyama, M.; To, T. L.; Yoshihara, K.; Gotoh, H.
    Immunology Letters, (September, 2000) Vol. 73, No. 2-3, pp. 194. print.
SO
    Meeting Info.: 24th European Immunology Meeting of the European Federation
    of Immunological Societies (EFIS). Poznan, Poland. September 23-26, 2000.
    European Federation of Immunological Societies.
    CODEN: IMLED6. ISSN: 0165-2478.
    Conference; (Meeting)
    Conference; Abstract; (Meeting Abstract)
LA
    English
    Entered STN: 1 Nov 2000
    Last Updated on STN: 10 Jan 2002
    Adhesion molecules and chemokines in granulomas by ***Mycobacterium***
    avium subspecies paratuberculosis in TNF alpha deficient mice.
      ***Momotani, E.*** ; Miyama, M.; To, T. L.; Yoshihara, K.; Gotoh, H.
    Major Concepts
       Immune System (Chemical Coordination and Homeostasis); Infection
    Diseases
            ***Mycobacterium*** avium paratuberculosis granuloma: bacterial
       disease, clinica; l signs, convalescence, pathological changes
    Chemicals & Biochemicals
       RANTES: granuloma expression; fibronectin: epithelioid granuloma. . .
ORGN .
       model, tumor necrosis factor-alpha deficiency, wild type
    Taxa Notes
       Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
       Rodents, Vertebrates
ORGN Classifier
           ***Mycobacteriaceae***
                                     08881
            ***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria; Bacteria; Microorganisms
    Organism Name
           ***Mycobacterium*** avium paratuberculosis: pathogen
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
    ANSWER 11 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
    STN
                                                       DUPLICATE 5
AN
    1993:373039 BIOSIS <<LOGINID::20080325>>
DN
    PREV199396058714
    Immunohistochemical distribution of S-100 alpha-positive cells in bovine
      ***mycobacterial*** and non- ***mycobacterial*** granulomas.
      ***Momotani, E.*** [Reprint author]; Kubo, M. [Reprint author];
```

AII ΙT

AII

```
Ishikawa, Y.; Matsubara, Y. [Reprint author]; Nakajima, Y.; Yoshino, T.
CS
    Natl. Inst. Anim. Health, 3-1-1, Kan-nondai, Tsukuba, 305, Japan
SO
    Journal of Comparative Pathology, (1993) Vol. 108, No. 3, pp. 291-301.
    CODEN: JCVPAR. ISSN: 0021-9975.
DT
    Article
LA.
    English
ED
    Entered STN: 6 Aug 1993
     Last Updated on STN: 6 Aug 1993
AB
     By means of immunohistochemistry, the distribution of the alpha-subunit
     (S-100-alpha) and the beta-subunit (S-100-beta) of S-100 protein was
     studied in bovine granulomas caused by Actinomyces bovis, Actinobacillus
     lignieresi, Actinomyces (Corynebacterium) pyogenes, Pseudomonas
     aeruginosa, Staphylococcus aureus, ***Mycobacterium*** bovis and
       ***Mycobacterium*** paratuberculosis. S-100-alpha-positive epithelioid
     cells or dendritic cells were scattered among the predominantly
     S-100-alpha-negative cells of the mononuclear phagocyte system (MPS).
     S-100-beta was not found in the MPS cells of granulomas but was observed
     in the endothelial cells of blood vessels. A positive reaction to S-100
     was also seen in normal cells in the lymphoid and mammary tissues.
       ***Mycobacterial*** granulomas contained more S-100-alpha-positive
cells
     than did non- ***mycobacterial***
                                         ones.
     Immunohistochemical distribution of S-100 alpha-positive cells in bovine
       ***mycobacterial*** and non- ***mycobacterial*** granulomas.
       ***Momotani, E.*** [Reprint author]; Kubo, M. [Reprint author];
AH
     Ishikawa, Y.; Matsubara, Y. [Reprint author]; Nakajima, Y.; Yoshino, T.
AB.
    . . S-100 protein was studied in bovine granulomas caused by Actinomyces
     bovis, Actinobacillus lignieresi, Actinomyces (Corynebacterium) pyogenes,
                                                    ***Mycobacterium***
     Pseudomonas aeruginosa, Staphylococcus aureus,
     bovis and ***Mycobacterium*** paratuberculosis. S-100-alpha-positive
     epithelioid cells or dendritic cells were scattered among the
     predominantly S-100-alpha-negative cells of the mononuclear phagocyte
     system (MPS).. . of blood vessels. A positive reaction to S-100 was
     also seen in normal cells in the lymphoid and mammary tissues.
      ***Mycobacterial*** granulomas contained more S-100-alpha-positive
cells
     than did non- ***mycobacterial*** ones.
Classifier
       Micrococcaceae 07702
        Gram-Positive Cocci; Eubacteria; Bacteria; Microorganisms
     Organism Name
        Micrococcaceae
     Taxa Notes
        Bacteria, Eubacteria, Microorganisms
ORGN Classifier
            ***Mvcobacteriaceae***
                                     08881
     Super Taxa
           ***Mycobacteria*** ; Actinomycetes and Related Organisms;
        Eubacteria; Bacteria; Microorganisms
     Organism Name
           ***Mycobacterium***
                                avium
     Taxa Notes
       Bacteria, Eubacteria, Microorganisms
ORGN Classifier
       Pasteurellaceae 06703
```

Super Taxa Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms Organism. . . ANSWER 12 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on DUPLICATE 6 1992:369927 BIOSIS <<LOGINID::20080325>> PREV199294051977; BA94:51977 IMMUNOHISTOCHEMICAL IDENTIFICATION OF FERRITIN LACTOFERRIN AND TRANSFERRIN IN LEPROSY LESIONS OF HUMAN SKIN BIOPSIES. \*\*\*MOMOTANI E\*\*\* [Reprint author]; WUSCHER N; RAVISSE P; RASTOGI N LAB IMMUNOPATHOL, NATIONAL INST ANIMAL HEALTH, 3-1-1 KANNONDAI, TSUKUBA, IBARAKI 305, JPN Journal of Comparative Pathology, (1992) Vol. 106, No. 3, pp. 213-220. CODEN: JCVPAR. ISSN: 0021-9975. Article ENGLISH Entered STN: 9 Aug 1992 Last Updated on STN: 9 Aug 1992 Granulomatous lesions of human leprosy contained ferritin and lactoferrin but little or no transferrin, as demonstrated by the avidin-biotin complex immunoperoxidase method. Lactoferrin was found in the neutrophils. These results suggested that the cells of the host mononuclear phagocyte system in leprosy granulomas provide an adequate nutritional environment for iron acquisition by \*\*\*Mycobacterium\*\*\* leprae. A possible role of iron binding proteins in the granulomas is discussed in relation to previous data on bovine paratuberculous granulomas. \*\*\*MOMOTANI E\*\*\* [Reprint author]; WUSCHER N; RAVISSE P; RASTOGI N AB. . . the cells of the host mononuclear phagocyte system in leprosy granulomas provide an adequate nutritional environment for iron acquisition by \*\*\*Mycobacterium\*\*\* leprae. A possible role of iron binding proteins in the granulomas is discussed in relation to previous data on bovine. . . Miscellaneous Descriptors \*\*\*MYCOBACTERIUM\*\*\* -LEPRAE NEUTROPHILS IRON BINDING PROTEINS ORGN Classifier \*\*\*Mvcobacteriaceae\*\*\* 08881 Super Taxa \*\*\*Mycobacteria\*\*\* ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms Taxa Notes Bacteria, Eubacteria, Microorganisms ORGN Classifier Hominidae 86215 Super Taxa Primates; Mammalia;. . . ANSWER 13 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on DUPLICATE 7 1991:182263 BIOSIS <<LOGINID::20080325>> PREV199191097012; BA91:97012 IMMUNOHISTOCHEMICAL STUDY OF BOVINE LYMPH NODES WITH ANTIBODIES AGAINST \$100 PROTEIN SUBUNITS COMPARISON BETWEEN LYMPH NODES OF HEALTHY AND \*\*\*MYCOBACTERIUM\*\*\* -PARATUBERCULOSIS INFECTED CATTLE.

\*\*\*MOMOTANI E\*\*\* [Reprint author]; YOSHINO T; ISHIKAWA Y; NAKAJIMA Y

T.2

AN

DM TT

TIA CS

SO

DT

FS LA

ED

AB

AU

L2

AN

DN

TΙ

AII

```
CS
    HOKKAIDO BRANCH LAB, NATL INST ANIM HEALTH, HITSUJIGAOKA-4, TOYOHIRA,
    SAPPORO 004, JPN
    Research in Immunology, (1990) Vol. 141, No. 8, pp. 771-782.
    CODEN: RIMME5. ISSN: 0923-2494.
DT
    Article
FS
    BA
T.A
    ENGLISH
ED
    Entered STN: 19 Apr 1991
    Last Updated on STN: 20 Apr 1991
AR
    Using immunohistochemistry, the differential distribution of the .alpha.
    subunit (S100.alpha.) and .beta. subunit (S100.beta.) of S100 protein was
    studied in mesenteric lymph nodes from normal or ***Mycobacterium***
    paratuberculosis-infected cattle. In epithelioid cell granulomas,
    S100.alpha.-positive epitheloid cells and some giant cells were scattered
    among $100.alpha.-negative cells, which were predominant. The
    S100.beta.-positive and -negative cells contained acid-fast bacilli. The
    presence of $100.beta.-positive cells was not demonstrated in the
    granulomas. In normal component cells in the lymph nodes, follicular
    dendritic cells in the germinal centres and endothelium of lymphatic sinus
    and lymph vessels were positive for $100.alpha.. $100.beta. was positive
    only in the endothelial cells of blood vessels. Results shown in the
    present paper are discussed in light of results obtained in other work on
    human tissues using the same sources of antibodies.
    IMMUNOHISTOCHEMICAL STUDY OF BOVINE LYMPH NODES WITH ANTIBODIES AGAINST
    S100 PROTEIN SUBUNITS COMPARISON BETWEEN LYMPH NODES OF HEALTHY AND
      ***MYCOBACTERIUM*** -PARATUBERCULOSIS INFECTED CATTLE.
      ***MOMOTANI E*** [Reprint author]; YOSHINO T; ISHIKAWA Y; NAKAJIMA Y
     . the .alpha. subunit (S100.alpha.) and .beta. subunit (S100.beta.) of
    S100 protein was studied in mesenteric lymph nodes from normal or
      ***Mycobacterium*** paratuberculosis-infected cattle. In epithelioid
    cell granulomas, $100.alpha.-positive epitheloid cells and some giant
    cells were scattered among $100.alpha.-negative cells, which were. . .
ORGN Classifier
           ***Mvcobacteriaceae***
                                     08881
    Super Taxa
           ***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria; Bacteria; Microorganisms
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
ORGN Classifier
       Bovidae
                85715
    Super Taxa
       Artiodactyla: Mammalia: . .
    ANSWER 14 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
                                                       DUPLICATE 8
ΔN
    1989:223916 BIOSIS <<LOGINID::20080325>>
DN
    PREV198987115533; BA87:115533
    IMMUNOHISTOCHEMICAL LOCALIZATION OF IMMUNOGLOBULINS IN BOVINE
TΙ
    GRANULOMATOUS LESIONS.
ΑU
      ***MOMOTANI E*** [Reprint author]; KUBO M; ISHIKAWA Y; YOSHINO T
CS
    HOKKAIDO BRANCH LAB, NATL INST ANIM HEALTH, HITSUJIGAOKA 4, TOYOHIRA,
```

Journal of Comparative Pathology, (1989) Vol. 100, No. 2, pp. 129-136.

DT Article FS BA

SO

SAPPORO 004 JPN

CODEN: JCVPAR. ISSN: 0021-9975.

```
LA ENGLISH
    Entered STN: 7 May 1989
ED
     Last Updated on STN: 7 May 1989
AB
   The immunohistochemical distribution of IgG, IgA and IgM in granulomatous
     lesions caused by Actinomyces boyis, Actinobacillus lignieresii,
     Actinomyces (Corynebacterium) pyogenes, Pseudomonas aeruginosa,
     Staphylococcus aureus and ***Mycobacterium*** boyis was studied.
     Numerous IgG-containing cells (plasma cells) were distributed in the
     peripheral connective tissue layers, but not in the epithelioid cell
     layer. A few scattered IgA- and IgM-containing cells were found in all
     the lesions examined. ***Mycobacterial*** granulomas contained fewer
     IGG-cells than did non- ***mycobacterial*** granulomas. Eosinophilic
     club-shaped bodies were found in A. bovis, A. lignieresi, P. aeruginosa
     and S. aureus, but they were generally negative for IgG, IgA and IgM.
AU
       ***MOMOTANI E*** [Reprint author]; KUBO M; ISHIKAWA Y; YOSHINO T
    . . IgA and IgM in granulomatous lesions caused by Actinomyces bovis,
ΔB
     Actinobacillus lignieresii, Actinomyces (Corynebacterium) pyogenes,
     Pseudomonas aeruginosa, Staphylococcus aureus and ***Mycobacterium***
     bovis was studied. Numerous IgG-containing cells (plasma cells) were
     distributed in the peripheral connective tissue layers, but not in the
     epithelioid cell layer. A few scattered IgA- and IgM-containing cells
     were found in all the lesions examined. ***Mycobacterial***
     granulomas contained fewer IgG-cells than did non- ***mycobacterial***
     granulomas. Eosinophilic club-shaped bodies were found in A. bovis, A.
     lignieresi, P. aeruginosa and S. aureus, but they were generally. . .
TT
    Miscellaneous Descriptors
       ACTINOMYCES-BOVIS ACTINOBACILLUS-LIGNIERESII ACTINOMYCES-PYOGENES
        PSEUDOMONAS-AERUGINOSA STAPHYLOCOCCUS-AUREUS ***MYCOBACTERIUM***
       -BOVIS IMMUNOGLOBULIN G IMMUNOGLOBULIN A IMMUNOGLOBULIN M PERIPHERAL
       CONNECTIVE TISSUE
ORGN . . .
       Nonsporing Gram-Positive Rods 08890
       Actinomycetes and Related Organisms; Eubacteria; Bacteria;
       Microorganisms
     Taxa Notes
        Bacteria, Eubacteria, Microorganisms
ORGN Classifier
           ***Mvcobacteriaceae***
                                    08881
     Super Taxa
            ***Mycobacteria*** ; Actinomycetes and Related Organisms;
        Eubacteria; Bacteria; Microorganisms
     Taxa Notes
        Bacteria, Eubacteria, Microorganisms
ORGN Classifier
       Bovidae 85715
     Super Taxa
       Artiodactyla; Mammalia;. . .
L2
    ANSWER 15 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
                                                       DUPLICATE 9
AN
     1988:483621 BIOSIS <<LOGINID::20080325>>
DN
    PREV198886114931; BA86:114931
TI
    THE DISTRIBUTION OF FERRITIN LACTOFERRIN AND TRANSFERRIN IN GRANULOMATOUS
     LYMPHADENITIS OF BOVINE PARATURERCULOSIS.
AU
       ***MOMOTANI E*** [Reprint author]; WHIPPLE D L; THIERMANN A B
```

HOKKAIDO BRANCH LAB, NATL INST ANIM HEALTH, HITSUJIGAOKA-4, SAPPORO 004

CS

```
.TPN
    Journal of Comparative Pathology, (1988) Vol. 99, No. 2, pp. 205-214.
SO
     CODEN: JCVPAR. ISSN: 0021-9975.
DT
    Article
FS
    ENGLISH
LA.
ED
    Entered STN: 1 Nov 1988
     Last Updated on STN: 1 Nov 1988
ΔR
     Immunohistochemical examination of iron-binding proteins was carried out
     in the formalin-fixed mesenteric lymph nodes of normal cattle and of
     cattle with paratuberculosis. Ferritin (FT) and lactoferrin (LF) were
     found in the granulomas in ileal lymph nodes from six infected cattle. A
     weak reaction for transferrin (TF) was found in granulomas of a lymph node
     from one of the infected cattle. FT was found in the macrophages in the
     medullary sinuses of normal and infected nodes; however, the reaction in
     infected nodes was generally stronger than that in normal ones. LF in the
    macrophages was found in only two infected nodes. Neutrophils in both
     normal and infected cattle always reacted strongly for LF. The TF was
     always found in the blood vessels and intracellular space. These results
     suggest that: (1) FT and LF may be important in vivo sources of iron for
       ***Mycobacterium*** paratuberculosis, since their own iron-binding
     compounds are considered to aquire iron from FT and LF in vitro; (2) the
     increase in FT and LF in the granulomas may be related to inflammatory
     hyposideraemia associated with paratuberculosis and (3) epithelioid and
     giant cells may have a different iron metabolism, from normal macrophages.
      ***MOMOTANI E*** [Reprint author]; WHIPPLE D L; THIERMANN A B
AU
AB.
     . . and intracellular space. These results suggest that: (1) FT and LF
     may be important in vivo sources of iron for ***Mycobacterium***
     paratuberculosis, since their own iron-binding compounds are considered to
     aguire iron from FT and LF in vitro; (2) the increase. . .
    Miscellaneous Descriptors
                ***MYCOBACTERIUM*** -PARATUBERCULOSIS MACROPHAGE NEUTROPHIL
        CATTLE
        HYPOSIDEREMIA
ORGN Classifier
            ***Mycobacteriaceae***
                                      08881
     Super Taxa
            ***Mycobacteria*** ; Actinomycetes and Related Organisms;
        Eubacteria; Bacteria; Microorganisms
     Taxa Notes
        Bacteria, Eubacteria, Microorganisms
ORGN Classifier
       Bovidae
                85715
     Super Taxa
        Artiodactyla; Mammalia;. . .
L2
    ANSWER 16 OF 20 CABA COPYRIGHT 2008 CABI on STN DUPLICATE 10
ΔN
     88:65054 CABA <<LOGINID::20080325>>
DN
     19882208990
TΙ
     Role of M cells and macrophages in the entrance of ***Mycobacterium***
     paratuberculosis into domes of ileal Peyer's patches in calves
ΑU
      ***Momotani, E.*** ; Whipple, D. L.; Thiermann, A. B.; Cheville, N. F.
    Nat. Anim. Dis. Center, PO Box 70, Ames, IA 50010, USA.
    Veterinary Pathology, (1988) Vol. 25, No. 2, pp. 131-137. 20 ref.
SO
    ISSN: 0300-9858
```

DT

LA English ED Entered

Journal

Entered STN: 1 Nov 1994

Last Updated on STN: 1 Nov 1994

AB Ligated ileal loops of calves inoculated with live and heat-killed M. paratuberculosis were examined by light and electron microscopy. At 5 hours after inoculation, acid-fast bacilli were in subepithelial macrophages, but not in M cells covering domes. At 20 hours, more than 50 acid-fast bacilli per cross section were in subepithelial macrophages in domes. Both living and heat-killed bacilli passed into domes. Addition of anti-M. paratuberculosis bovine serum to the inoculum increased entry of bacteria into domes. Electron microscopy showed intact bacilli with electron-transparent zones (peribacillary spaces) in the supranuclear cytoplasm of M cells at 20 hours. M cells also contained vacuoles, including electron-dense material interpreted as degraded bacilli. Subepithelial and intraepithelial macrophages contained bacilli and degraded bacterial material in phagosomes. These results suggest that calf ileal M cells take up bacilli, and that subepithelial and intraepithelial macrophages secondarily accept bacilli or bacterial debris which are expelled from M cells.

- TI Role of M cells and macrophages in the entrance of \*\*\*Mycobacterium\*\*\*
  paratuberculosis into domes of ileal Pever's patches in calves.
- AU \*\*\*Momotani, E.\*\*\* ; Whipple, D. L.; Thiermann, A. B.; Cheville, N. F.
- BT mammals; vertebrates; Chordata; animals; young animals;

  \*\*\*Mycobacterium\*\*\* ; \*\*\*Mycobacteriaceae\*\*\* ; Firmicutes; bacteria;
  prokaryotes
- ORGN \*\*\*Mycobacterium\*\*\* paratuberculosis; cattle
- L2 ANSWER 17 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 11
- AN 1987:106473 BIOSIS <<LOGINID::20080325>>
- DN PREV198783055451; BA83:55451
- TI IMMUNOHISTOCHEMICAL DISTRIBUTION OF IMMUNOGLOBULIN AND SECRETORY COMPONENT IN THE ILEUM OF NORMAL AND PARATUBERCULOSIS-INFECTED CATTLE.
- AU \*\*\*MOMOTANI E\*\*\* [Reprint author]; ISHIKAWA Y; YOSHINO T CS HOKKAIDO BRANCH LABORATORY, NATIONAL INSTITUTE OF ANIMAL HEALTH,
- HITSUJIGAOKA 4, TOYOHIRA-KU, SAPPORO 004, JAPAN
- SO Journal of Comparative Pathology, (1986) Vol. 96, No. 6, pp. 659-670. CODEN: JCVPAR. ISSN: 0021-9975.
- DT Article
- FS BA LA ENGLISH
- ED Entered STN: 26 Feb 1987
  - Last Updated on STN: 26 Feb 1987
- AB The immunohistochemical distribution of IqA, IqG, IqM and secretory component in the ileum of 10 normal and 21 paratuberculosis-infected cattle was investigated. Semi-quantitative analysis of the number of each class of Ig-containing cells in the lamina propria mucosa of infected ileums showed that IgG and IgM-containing cells and total Ig-containing cells were significantly more numerous than those in the normal ileums. There was no significant difference in the numbers of IgA-containing cells between the two groups of cattle. The distribution of IgA, IgM and SC was basically similar in the two groups. However, IgG-containing cells characteristically accumulated around the granulomas. It was considered that excessive local production of Ig in the intestinal mucosa, along with subsequent formation of immune complex or release of histamine from mast cells, could account for the occurrence of diarrhoea and participate in the pathogenesis of bovine paratuberculosis. A comparison of the local immunological state in paratuberculosis and Crohn's disease was made.

```
ORGN Classifier
            ***Mycobacteriaceae*** 08881
     Super Taxa
            ***Mycobacteria*** ; Actinomycetes and Related Organisms;
        Eubacteria: Bacteria: Microorganisms
     Taxa Notes
        Bacteria, Eubacteria, Microorganisms
ORGN Classifier
       Bovidae
                85715
     Super Taxa
       Artiodactyla; Mammalia;. . .
L2
    ANSWER 18 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
                                                       DUPLICATE 12
AN
    1986:281052 BIOSIS <<LOGINID::20080325>>
    PREV198682024915; BA82:24915
DN
тт
     IMMUNOHISTOCHEMICAL DISTRIBUTION OF FERRITIN LACTOFERRIN AND TRANSFERRIN
     IN GRANULOMAS OF BOVINE PARATUBERCULOSIS.
       ***MOMOTANI E*** [Reprint author]; FURUGOURI K; OBARA Y; MIYATA Y;
ΑU
     ISHIKAWA Y; YOSHINO T
CS
     HAKKAIDO BRANCH LABORATORY, NATIONAL INSTITUTE OF ANIMAL HEALTH,
    HITSUJIGAOKA, TOYOHIRA-KU, SAPPORO 004, JAPAN
     Infection and Immunity, (1986) Vol. 52, No. 2, pp. 623-627.
SO
    CODEN: INFIBR. ISSN: 0019-9567.
DT
    Article
FS
    BA
LA
    ENGLISH
   Entered STN: 4 Jul 1986
ED.
     Last Updated on STN: 4 Jul 1986
AB Granulomatous lesions of bovine paratuberculosis contained ferritin,
     lactoferrin and a small amount of transferrin, as demonstrated by the
     immunohistochemical method. Macrophages in the normal bovine ileum did
    not contain lactoferrin and transferrin; however, ferritin was found in
     individual macrophages of Peyer's patches. These results may help
     elucidate the relationship between intracellular growth of
      ***Mycobacterium*** paratuberculosis and the presence of iron-binding
     proteins in the granulomas.
ΑU
      ***MOMOTANI E***
                        [Reprint author]; FURUGOURI K; OBARA Y; MIYATA Y;
    ISHIKAWA Y; YOSHINO T
AB.
     . . ferritin was found in individual macrophages of Peyer's patches.
    These results may help elucidate the relationship between intracellular
    growth of ***Mycobacterium*** paratuberculosis and the presence of
     iron-binding proteins in the granulomas.
   Miscellaneous Descriptors
            ***MYCOBACTERIUM*** -PARATUBERCULOSIS ***MYCOBACTIN***
EXOCHELIN
        IRON-BINDING PROTEIN INTRACELLULAR GROWTH ENTERITIS
ORGN Classifier
           ***Mycobacteriaceae***
                                     08881
     Super Taxa
            ***Mycobacteria*** ; Actinomycetes and Related Organisms;
        Eubacteria; Bacteria; Microorganisms
     Taxa Notes
       Bacteria, Eubacteria, Microorganisms
ORGN Classifier
       Bovidae 85715
     Super Taxa
```

```
Artiodactyla; Mammalia;.
    1400-46-0 ( ***MYCOBACTIN*** )
RN
    ANSWER 19 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
L2
                                                       DUPLICATE 13
    1985:408087 BIOSIS <<LOGINID::20080325>>
AN
DM
    PREV198580078079; BA80:78079
ТT
    CASEOUS GRANULOMAS IN BOVINE PARATUBERCULOSIS.
AU
      ***MOMOTANI E*** [Reprint author]; YOSHINO T
CS
    HODDAIDO BRANCH LABORATORY, NATIONAL INSTITUTE OF ANIMAL HEALTH, 4
    HITSUJIGAOKA, TOYOHIRA-KU, SAPPORO 061-01, JAPAN
SO
    Japanese Journal of Veterinary Science, (1985) Vol. 47, No. 3, pp.
    487-492.
    CODEN: NJUZA9. ISSN: 0021-5295.
DT
    Article
FS
I.A
    ENGLISH
    Caseous granulomas were found in the mesenteric lymph nodes of an
    Aberdeen-Angus cow, 5 vr old, having paratuberculosis. They were found
    together with epithelioid cell granulomas, and both of them contained
    numerous acid-fast bacilli. The intestine showed extensive
    paratuberculous lesions with numerous acid-fast bacilli. There was no
    caseation but focal neutrophil infiltration in the intestinal granulomas.
      ***Mycobacterium*** paratuberculosis was isolated from both the
    mesenteric lymph nodes and the intestine. No tuberculous bacilli were
    detected, and tuberculin and Johnin tests were negative.
AU
      ***MOMOTANI E*** [Reprint author]; YOSHINO T
AR.
     . . showed extensive paratuberculous lesions with numerous acid-fast
    bacilli. There was no caseation but focal neutrophil infiltration in the
    intestinal granulomas. ***Mycobacterium*** paratuberculosis was
    isolated from both the mesenteric lymph nodes and the intestine. No
    tuberculous bacilli were detected, and tuberculin and. . .
    Miscellaneous Descriptors
            ***MYCOBACTERIUM*** -PARATUBERCULOSIS INTESTINAL PARATUBERCULOUS
       LESIONS ACID-FAST BACILLI FOCAL NEUTROPHIL INFILTRATION
ORGN Classifier
           ***Mvcobacteriaceae***
                                     08881
    Super Taxa
           ***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria; Bacteria; Microorganisms
       Bacteria, Eubacteria, Microorganisms
ORGN Classifier
       Bovidae
                85715
    Super Taxa
       Artiodactyla; Mammalia; . . .
L2
    ANSWER 20 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
                                                       DUPLICATE 14
AN
    1985:279500 BIOSIS <<LOGINID::20080325>>
DN
    PREV198579059496; BA79:59496
TI
    PATHOLOGICAL CHANGES OF SPONTANEOUS DUAL INFECTION OF TUBERCULOSIS AND
    PARATUBERCULOSIS IN BEEF CATTLE.
AU
      ***MOMOTANI E*** [Reprint author]; YOSHINO T
CS
    HOKKAIDO BRANCH LAB, NATL INST ANIMAL HEALTH, 4 HITSUJIGAOKA, TOYOHIRA-KU,
    SAPPORO, HOKKAIDO 061-01, JPN
    Japanese Journal of Veterinary Science, (1984) Vol. 46, No. 5, pp.
SO
```

```
625-632
    CODEN: NJUZA9. ISSN: 0021-5295.
    Article
FS
LA ENGLISH
AB Four cases of spontaneous dual infection of tuberculosis and
    paratuberculosis in beef cattle, first noticed in Japan, were examined
    pathologically. All of the cattle were from the same limited area of
     Hokkaido island. Tuberculous lesions were found in 2-9 organs, including
     the liver, lung, kidney and mesenteric lymph nodes, and granulomas showed
     the same appearance as in the case of single infection. Paratuberculous
     lesions characterized by intracellular short acid-fast bacilli were found
     in the jejunum, ileum, cecum and the draining lymp nodes, but they were
    not severe. The mesenteric lymph nodes revealed both tuberculous and
    paratuberculous lesions, and in 2 of the 4 cases both types of granulomas
    were present in the same sections. In such sections, short acid-fast
     bacilli were not numerous in granulomas adjacent to tuberculous lesions.
       ***MOMOTANI E*** [Reprint author]; YOSHINO T
ORGN Classifier
            ***Mycobacteriaceae***
                                     08881
     Super Taxa
           ***Mycobacteria*** ; Actinomycetes and Related Organisms;
        Eubacteria: Bacteria: Microorganisms
        Bacteria, Eubacteria, Microorganisms
ORGN Classifier
        Bovidae 85715
     Super Taxa
       Artiodactyla; Mammalia;. . .
=> e mori yasuyuki/au
E1
           58
               MORI YASUYOSHI/AU
E2
            1
                 MORI YASUYOSMI/AU
E3
          175 --> MORI YASUYUKI/AU
E4
                 MORI YASUZANE/AU
           1
E5
           12
                 MORI YAYOI/AU
          233 MORI YO/AU
1 MORI YO ICHI/AU
E6
E7
E8
            1
                 MORI YOHIRO/AU
E9
            4
                 MORT YORKO/AII
E10
            3
                 MORI YOHTA/AU
E11
          311 MORI YOICHI/AU
56 MORI YOICHIRO/AU
E12
=> s e3 and mycobact?
           33 "MORI YASUYUKI"/AU AND MYCOBACT?
=> dup rem 13
PROCESSING COMPLETED FOR L3
            15 DUP REM L3 (18 DUPLICATES REMOVED)
=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):v
L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:428046 CAPLUS <<LOGINID::20080325>>
```

- DN 146:416306
- Primer sets for detection of expression level of urocortin for evaluation of progressing of johne's disease in livestock
- IN Momotani, Eiichi; \*\*\*Mori, Yasuyuki\*\*\* ; Wang, Hong Yu
- PA National Agriculture Bio-Oriented Research Organization, Japan
- SO Jpn. Kokai Tokkyo Koho, 15pp. CODEN: JKXXAF
- DT Patent
- LA Japanese
- FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
PI	JP 2007097490	A	20070419	JP 2005-291868	20051005		
PRAT	.TP 2005-291868		20051005				

- AB This invention provides primer sets for detection of expression level of urcocrtin in livestock blood sample by realtime-PCR. The cDNA sequence of Bos taurus urcocrtin were disclosed. The invention also provides method for prepn. of std. curve for real-time PCR by detecting the expression level of urcocrtin gene in Bos taurus cells immunized with antigen from \*\*\*Mycobacterium\*\*\* paratuberculosis. The method provided in this invention can be used for evaluation of progressing of johne's disease in livestock in early stage of infection.
- IN Momotani, Eiichi; \*\*\*Mori, Yasuyuki\*\*\* ; Wang, Hong Yu
- AB . . . curve for real-time PCR by detecting the expression level of urocortin gene in Bos taurus cells immunized with antigen from \*\*\*Bycobacterium\*\*\* paratuberculosis. The method provided in this invention can be used for evaluation of progressing of johne's disease in livestock in . .
- IT \*\*\*Mycobacterium\*\*\* avium paratuberculosis
  (infection of; primer sets for detection of expression level of
  - (injection of; primer sets for detection of expression level of uncoording for evaluation of progressing of johne's disease in livestock)
- L4 ANSWER 2 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on SIN DUPLICATE 1
- AN 2007:589654 BIOSIS <<LOGINID::20080325>>
- DN PREV200700590889
- TI Corticotropin-releasing hormone and urocortin expression in peripheral blood cells from experimentally infected cattle with \*\*\*Mycobacterium\*\*\* avium subsp paratuberculosis.
- AU Wang, Hongyu; Aodon-geril; Shu, Yujing; Momotani, Yuriko; Wang, Xiaofei; \*\*\*Mori, Yasuyuki\*\*\* ; Momotani, Eiichi [Reprint Author]
- CS Natl Inst Anim Hlth, Res Team Paratuberculosis, 3-1-5 Kan-nondai, Tsukuba, Ibaraki 3050856, Japan momotani@affrc.go.jp
- SO Microbes and Infection, (JUL 2007) Vol. 9, No. 9, pp. 1061-1069. ISSN: 1286-4579.
- DT Article
- LA English
- ED Entered STN: 21 Nov 2007
  - Last Updated on STN: 21 Nov 2007
- AB Urocortin (UCN) is a new neuropeptide of the corticotrophin-releasing hormone (CRR) family which plays an important role in immune responses.

  \*\*\*Mycobacterium\*\*\* a wium subspecies paratuberculosis (Map) is the etiological agent of paratuberculosis (Johne's disease). The role of UCN or CRH in the pathogenesis of Map-infection is unknown. In the present study, we first cloned the bovine UCN gene and demonstrated the profile of

UCN or CRH expression in peripheral blood cells from Map-infected cattle and uninfected controls by real-time reverse transcription-polymerase chain reaction (RT-PCR) and ELISA analysis. These data are the first observations of the characteristic kinetics of these neuropeptides in Map-infection. UCN or CRH expression in non-stimulated blood samples from infected cattle was higher than that in similarly treated samples from uninfected controls; however, exposure to Map lysate and live Map resulted in down-regulated expression of UCN in infected cattle compared to their counterparts from uninfected controls. These results have provided a direction in understanding the pathogenesis of paratuberculosis and improving diagnostic methods for Map-infection. (C) 2007 Elsevier Masson SAS. All rights reserved.

- Corticotropin-releasing hormone and urocortin expression in peripheral blood cells from experimentally infected cattle with \*\*\*Mycobacterium\*\*\* avium subsp paratuberculosis.
- Wang, Hongyu; Aodon-geril; Shu, Yujing; Momotani, Yuriko; Wang, Xiaofei; \*\*\*Mori, Yasuyuki\*\*\* ; Momotani, Eiichi [Reprint Author]
- AB. . . Urocortin (UCN) is a new neuropeptide of the corticotrophinreleasing hormone (CRH) family which plays an important role in immune \*\*\*Mycobacterium\*\*\* avium subspecies paratuberculosis (Map) is the etiological agent of paratuberculosis (Johne's disease). The role of UCN or CRH in the. . .
- ORGN . . . Chordata; Animalia

Organism Name

bovine (common): host

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

ORGN Classifier

\*\*\*Mycobacteriaceae\*\*\*

Super Taxa

08881 \*\*\*Mycobacteria\*\*\* ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms

Organism Name

\*\*\*Mycobacterium\*\*\* avium paratuberculosis (subspecies): pathogen Taxa Notes

Bacteria, Eubacteria, Microorganisms

- L4 ANSWER 3 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 2
- AN 2008:30137 BIOSIS <<LOGINID::20080325>>
- DN PREV200800031655
- Detection of \*\*\*Mycobacterium\*\*\* avium subsp paratuberculosis in ovine faeces by direct quantitative PCR has similar or greater sensitivity compared to radiometric culture.
- AU Kawaji, Satoko; Taylor, Deborah L.; \*\*\*Mori, Yasuyuki\*\*\* ; Whittington, Richard J. [Reprint Author]
- Univ Sydney, Fac Vet Sci, 425 Werombi Rd, Camden, NSW 2570, Australia CS richardw@camden.usyd.edu.au
- Veterinary Microbiology, (NOV 15 2007) Vol. 125, No. 1-2, pp. 36-48. SO CODEN: VMICDQ. ISSN: 0378-1135.
- Article
- LA English
- Entered STN: 19 Dec 2007 ED
  - Last Updated on STN: 19 Dec 2007
- AB The aims of this study were to develop a new real-time quantitative PCR

(QPCR) assay based on IS900 for detection and quantification of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis (MAP) DNA in faeces, and to use this to detect infected sheep. Both the C and S strains of MAP were detected by the QPCR assay, and no cross reactions were detected with 51 other species of \*\*\*mycobacteria\*\*\* including 10 which contained IS900-like sequences. One copy of IS900 fragment cloned into plasmid pCR2.1 and 1 fg of MAP genomic DNA were consistently detected, while in spiked faecal samples the detection limit was 10 viable MAP per gram of ovine faeces. A total of 506 individual ovine faecal samples and 27 pooled ovine faecal samples with known culture results were tested. The QPCR assay detected 68 of 69 BACTEC culture positive individual faeces and there was a strong relation between time to detection in culture and DNA quantity measured by QPCR (r = -0.70). In pooled faecal samples, QPCR also agreed with culture (kappa = 0.59). MAP DNA was detected from some culture negative faecal samples from sheep exposed to MAP, suggesting that the QPCR has very high analytical sensitivity for MAP in faecal samples and detects non-viable MAP in ovine faeces. None of the faecal samples from 176 sheep that were not exposed to MAP were positive in QPCR. This is the first report of a direct faecal OPCR assay that has similar sensitivity to a gold standard radiometric culture assay. (C) 2007 Elsevier B.V. All rights reserved.

- TI Detection of \*\*\*MyCobacterium\*\*\* avium subsp paratuberculosis in ovine faeces by direct quantitative PCR has similar or greater sensitivity compared to radiometric culture.
- AU Kawaji, Satoko; Taylor, Deborah L.; \*\*\*Mori, Yasuyuki\*\*\*; Whittington, Richard J. [Reprint Author]
- AB. . this study were to develop a new real-time quantitative PCR (QPCR) assay based on IS900 for detection and quantification of 
  \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis (MAP) DNA in faeces, and to use this to detect infected sheep. Both the C and S. . strains of MAP were detected by the QPCR assay, and no cross reactions were detected with 51 other species of 
  \*\*\*mycobacteria\*\*\* including 10 which contained IS900-like sequences. One copy of IS900 fragment cloned

ORGN . . . Chordata: Animalia

Organism Name

ovine (common): host

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

ORGN Classifier

\*\*\*Mycobacteriaceae\*\*\* 08881

Super Taxa

\*\*\*Mycobacteria\*\*\* ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms

Organism Name

\*\*\*Mycobacterium\*\*\* avium paratuberculosis (subspecies): pathogen
Taxa Notes

Bacteria, Eubacteria, Microorganisms

into plasmid pCR2.1 and 1 fg of MAP. . .

- L4 ANSWER 4 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 3
- AN 2006:532033 BIOSIS <<LOGINID::20080325>>
- DN PREV200600524060
- TI A highly sensitive and subspecies-specific surface antigen enzyme-linked immunosorbent assay for diagnosis of Johne's disease.

AU Eda, Shigetoshi; Bannantine, John P.; Waters, W. R.; \*\*\*Mori, \*\*\* Yasuyuki\*\*\* ; Whitlock, Robert H.; Scott, M. Cathy; Speer, C. A. Reprint

Author]

- Univ Tennessee, Ctr Wildlife Hlth, Dept Forestry Wildlife and Fisheries, POB 1071, Knoxville, TN 37901 USA caspeer@utk.edu
- Clinical and Vaccine Immunology, (AUG 2006) Vol. 13, No. 8, pp. 837-844. SO ISSN: 1556-6811.
- Article
- LA English
- Entered STN: 12 Oct 2006 ED
  - Last Updated on STN: 12 Oct 2006
- Johne's disease (JD), or paratuberculosis, caused by \*\*\*Mycobacterium\*\*\* AB avium subsp. paratuberculosis, is one of the most widespread and economically important diseases of livestock and wild ruminants worldwide. Control of JD could be accomplished by diagnosis and good animal husbandry, but this is currently not feasible because commercially available diagnostic tests have low sensitivity levels and are incapable of diagnosing prepatent infections. In this study, a highly sensitive and subspecies-specific enzyme-linked immunosorbent assay was developed for the diagnosis of JD by using antigens extracted from the surface of M. avium subsp. paratuberculosis. Nine different chemicals and various intervals of agitation by vortex were evaluated for their ability to extract the surface antigens. Various quantities of surface antigens per well in a 96-well microtiter plate were also tested. The greatest differences in distinguishing between JD-positive and JD-negative serum samples by ethanol vortex enzyme-linked immunosorbent assav (EVELISA) were obtained with surface antigens dislodged from 50 mu g/well of bacilli treated with 80% ethanol followed by a 30-second interval of agitation by vortex. The diagnostic specificity and sensitivity of the EVELISA were 97.4% and 100%, respectively. EVELISA plates that had been vacuum-sealed and then tested 7 weeks later (the longest interval tested) had diagnostic specificity and sensitivity rates of 96.9 and 100%, respectively. In a comparative study involving serum samples from 64 fecal culture-positive cattle, the EVELISA identified 96.6% of the low-level fecal shedders and 100% of the midlevel and high-level shedders, whereas the Biocor ELISA detected 13.7% of the low-level shedders, 25% of the mid-level shedders, and 96.2% of the high-level shedders. Thus, the EVELISA was substantially superior to the Biocor ELISA, especially in detecting low-level and midlevel shedders. The EVELISA may form the basis for a highly sensitive and subspecies-specific test for the diagnosis of JD.
- AU Eda, Shigetoshi; Bannantine, John P.; Waters, W. R.; \*\*\*Mori, \*\*\* Yasuyuki\*\*\* ; Whitlock, Robert H.; Scott, M. Cathy; Speer, C. A.

[Reprint

Author]

Johne's disease (JD), or paratuberculosis, caused by \*\*\*Mvcobacterium\*\*\* avium subsp. paratuberculosis, is one of the most widespread and economically important diseases of livestock and wild ruminants worldwide. Control. .

Organism Name

bovine (common): host, cattle, female

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

ORGN Classifier

\*\*\*Mycobacteriaceae\*\*\* 08881

Super Taxa

\*\*\*Mycobacteria\*\*\* ; Actinomycetes and Related Organisms;

Eubacteria; Bacteria; Microorganisms

Organism Name

 $$^{***}\mbox{Mycobacterium}^{***}$$  avium paratuberculosis (subspecies): pathogen Taxa Notes

Bacteria, Eubacteria, Microorganisms

- L4 ANSWER 5 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 4
- AN 2006:467815 BIOSIS <<LOGINID::20080325>>
- DN PREV200600465331
- TI A novel enzyme-linked immunosorbent assay for diagnosis of \*\*\*Mycobacterium\*\*\* avium subsp paratuberculosis infections (Johne's disease) in cattle.
- AU Speer, C. A. [Reprint Author]; Scott, M. Cathy; Bannantine, John P.; Waters, W. Ray; \*\*\*Mori, Yasuyuki\*\*\*; Whitlock, Robert H.; Eda, Shicetoshi
- CS Univ Tennessee, Dept Forestry Wildlife and Fisheries, Ctr Wildlife Hlth, POB 1071, Knoxville, TN 37901 USA caspeer@utk.edu
- SO Clinical and Vaccine Immunology, (MAY 2006) Vol. 13, No. 5, pp. 535-540. ISSN: 1556-6811.
- DT Article
- LA English
- ED Entered STN: 20 Sep 2006
  - Last Updated on STN: 20 Sep 2006
- AB Enzyme-linked immunosorbent assays (ELISAs) for the diagnosis of Johne's disease (JD), caused by \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis, were developed using whole bacilli treated with formaldehyde (called WELISA) or surface antigens obtained by treatment of H. avium subsp. paratuberculosis bacilli with formaldehyde and then brief sonication (called SELISA). ELISA plates were coated with either whole bacilli or sonicated antigens and tested for reactivity against serum obtained from JD-positive and JD-negative cattle or from calves experimentally inoculated with M. avium subsp. paratuberculosis,
  - \*\*Mycobacterium\*\*\* avium subsp. avium, or \*\*\*Mycobacterium\*\*\* bovis. Because the initial results obtained from the WELISA and SELISA were similar, most of the subsequent experiments reported herein were performed using the SELISA method. To optimize the SELISA test, various concentrations (3.7 to 37%) of formaldehyde and intervals of sonication (2 to 300 s) were tested. With an increase in formaldehyde concentration and a decreased interval of sonication, there was a concomitant decrease in nonspecific binding by the SELISA. SELISAs prepared by treating M. avium subsp. paratuberculosis with 37% formaldehyde and then a 2-s burst of sonication produced the greatest difference (TX) between M. avium subsp. paratuberculosis-negative and M. avium subsp. paratuberculosis-positive serum samples. The diagnostic sensitivity and specificity for JD by the SELISA were greater than 95%. The SELISA showed subspecies-specific detection of M. avium subsp. paratuberculosis in calves experimentally inoculated with M. avium subsp. paratuberculosis or other
  - \*\*\*mycobacteria\*\*\* . Based on diagnostic sensitivity and specificity, the SELISA appears superior to the commercial ELISAs routinely used for the diagnosis of JD.
- TI A novel enzyme-linked immunosorbent assay for diagnosis of

  \*\*\*Mycobacterium\*\*\* avium subsp paratuberculosis infections (Johne's

```
disease) in cattle.
AU
    Speer, C. A. [Reprint Author]; Scott, M. Cathy; Bannantine, John P.;
    Waters, W. Ray: ***Mori, Yasuvuki***; Whitlock, Robert H.; Eda,
    Shigetoshi
    Enzyme-linked immunosorbent assays (ELISAs) for the diagnosis of Johne's
AR
    disease (JD), caused by ***Mycobacterium*** avium subsp.
    paratuberculosis, were developed using whole bacilli treated with
    formaldehyde (called WELISA) or surface antigens obtained by treatment of.
     . . for reactivity against serum obtained from JD-positive and
    JD-negative cattle or from calves experimentally inoculated with M. avium
    subsp. paratuberculosis, ***Mycobacterium*** avium subsp. avium, or
      ***Mycobacterium*** bovis. Because the initial results obtained from
    the WELISA and SELISA were similar, most of the subsequent experiments
    reported herein. . . showed subspecies-specific detection of M. avium
    subsp. paratuberculosis infections in calves experimentally inoculated
    with M. avium subsp. paratuberculosis or other ***mycobacteria*** .
    Based on diagnostic sensitivity and specificity, the SELISA appears
    superior to the commercial ELISAs routinely used for the diagnosis of. .
ΙT
    Major Concepts
       Infection; Methods and Techniques
IT
    Diseases
           ***Mycobacterium*** avium tuberculosis infection: bacterial
       disease, infectious disease, diagnosis, Johne's disease
    Chemicals & Biochemicals
       formaldehyde; surface antigen
ORGN .
       Chordata; Animalia
    Organism Name
       cattle (common): host
    Taxa Notes
       Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,
       Nonhuman Mammals, Vertebrates
ORGN Classifier
           ***Mycobacteriaceae***
                                    08881
    Super Taxa
           ***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria; Bacteria; Microorganisms
    Organism Name
           ***Mycobacterium***
                               bovis (species)
           ***Mvcobacterium***
                               avium paratuberculosis (subspecies): pathogen
           ***Mycobacterium*** avium avium (subspecies)
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
T.4
    ANSWER 6 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
    AN
DN
    142:334896
TΙ
    Method for diagnosing johne's disease
IN
    Momotani, Eiichi; ***Mori, Yasuyuki*** ; Hikono, Hirokazu; Buza, Joram
    Josephat
PA
    Incorporated Administrative Agency National Agriculture and Bio-Oriented
    Research Organization, Japan
```

DT Patent

Japanese

PCT Int. Appl., 38 pp. CODEN: PIXXD2

SO

L.A

FAN.CNT	1
---------	---

	PATE	ENT 1	10.			KIN	)	DATE			APPL	ICAT	ION	NO.		D.	ATE	
							-									-		
PI	WO 2	20050	290	79		A1		2005	0331		WO 2	003-	JP11	845		2	0030	917
		W:	AU,	JP,	US													
		RW:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,
			IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR						
	AU 2	20032	2728	80		A1		2005	0411		AU 2	003-	2728	80		2	0030	917
	US 3	20080	387	58		A1		2008	0214		US 2	007-	5725	14		2	0070	426
	***	2002	TD4			-		2002	0000									

PRAI WO 2003-JP11845 20030917 AB A method for diagnosing johne's disease is provided, with which an animal infected with \*\*\*Mycobacterium\*\*\* paratuberculosis (Johne's) can be diagnosed at a high sensitivity in the inapparent infection stage before the specific antibody level begins to increase, and a large no. of specimens can be treated. The method is characterized in that it comprises collecting a blood sample of a subject animal, adding an anti-IL-10 antibody and a \*\*\*Mycobacterium\*\*\* paratuberculosis antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma, vield in the cultured blood. The method is also characterized in that the IFN.gamma. yield in blood is measured by the IFN.gamma. ELISA method. Also provided is a method for diagnosing \*\*\*mycobacteriosis\*\*\* , which is characterized by comprising collecting a blood sample of a subject animal, adding an anti-IL-10 antibody and a \*\*\*Mycobacterium\*\*\* antigen to the collected blood followed by culturing, and then, measuring

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

the IFN.gamma. yield in the cultured blood.

IN Momotani, Eiichi; \*\*\*Mori, Yasuyuki\*\*\* ; Hikono, Hirokazu; Buza, Joram Josephat

NB A method for diagnosing johne's disease is provided, with which an animal infected with "\*\*Mycobacterium\*\*\* paratuberculosis (Johne's) can be diagnosed at a high sensitivity in the inapparent infection stage before the specific antibody level begins. . . is characterized in that it comprises collecting a blood sample of a subject animal, adding an anti-TL-10 antibody and a "\*\*Mycobacterium\*\*\* paratuberculosis antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma. yield in the cultured blood. The. . . that the IFN.gamma yield in blood is measured by the IFN.gamma. ELISA method. Also provided is a method for diagnosing "\*\*mycobacteriosis\*\*\*, which is characterized by comprising collecting a blood sample of a subject animal, adding an anti-TL-10 antibody and a "\*Mycobacterium\*\*\* antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma. yield in the cultured blood.

IT Animals

Blood analysis

Diagnosis

\*\*\*Mycobacterium\*\*\* avium paratuberculosis

(method for diagnosing johne's disease by measuring blood IFN.gamma. by ELISA)

- L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2005:315731 CAPLUS <<LOGINID::20080325>>
- DN 142:390942
- TI Protein and DNA sequence of \*\*\*Mycobacterium\*\*\* johnei antigens able to induce interferon and uses in diagnosis
- IN \*\*\*Mori, Yasuyuki\*\*\*; Nagata, Reiko; Yoshihara, Kazuhiro; Sota, Yoshihiro; Yokomizo, Yuichi

- National Institute of Agro-Environmental Sciences, Japan
- Jpn. Kokai Tokkyo Koho, 12 pp. SO
- CODEN: JKXXAF
- DT Patent
- LA Japanese
- FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
PI	JP 2005095101	A	20050414	JP 2003-334977	20030926		
	JP 3864230	B2	20061227				
PRAI	JP 2003-334977		20030926				

- AB The sequences of antigens able to induce interferon .gamma. are isolated from cow PBMC (peripheral blood mononuclear cell) infected with

  - \*\*\*Mycobacterium\*\*\* johnei. The induction of interferon .gamma. by \*\*\*Mycobacterium\*\*\* johnei is useful in diagnosis of infection of \*\*\*Mycobacterium\*\*\* johnei by detection of interferon .gamma. in the supernatant of infected cells.
  - Protein and DNA sequence of \*\*\*Mycobacterium\*\*\* johnei antigens able to induce interferon and uses in diagnosis
- IN \*\*\*Mori, Yasuyuki\*\*\* ; Nagata, Reiko; Yoshihara, Kazuhiro; Sota, Yoshihiro; Yokomizo, Yuichi
- AB The sequences of antigens able to induce interferon .gamma. are isolated from cow PBMC (peripheral blood mononuclear cell) infected with
  - \*\*\*Mycobacterium\*\*\* johnei. The induction of interferon .gamma. by
    \*\*\*Mycobacterium\*\*\* johnei is useful in diagnosis of infection of
  - \*\*\*Mycobacterium\*\*\* johnei by detection of interferon .gamma. in the supernatant of infected cells.
- ST \*\*\*Mycobacterium\*\*\* antigen sequence interferon gamma induction
- IT Mononuclear cell (leukocyte)
  - (PBMC; protein and DNA sequence of \*\*\*Mycobacterium\*\*\* antigens able to induce interferon and uses in diagnosis)
- ΤТ Animal cell (diagnostic sample from; protein and DNA sequence of

  - \*\*\*Mycobacterium\*\*\* johnei antigens able to induce interferon and uses in diagnosis)
- Gene, microbial ΙT
  - RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
    - (encoding antigen; protein and DNA sequence of \*\*\*Mycobacterium\*\*\* johnei antigens able to induce interferon and uses in diagnosis)
- TT Diagnosis
  - (mol.; protein and DNA sequence of \*\*\*Mycobacterium\*\*\*
  - antigens able to induce interferon and uses in diagnosis)
- IT Infection
  - (of \*\*\*Mycobacterium\*\*\* johnei, diagnosis of; protein and DNA sequence of \*\*\*Mycobacterium\*\*\* johnei antigens able to induce interferon and uses in diagnosis)
- Bos taurus
  - DNA sequences
    - \*\*\*Mycobacterium\*\*\* avium paratuberculosis
    - Protein sequences
    - (protein and DNA sequence of \*\*\*Mycobacterium\*\*\* johnei antigens able to induce interferon and uses in diagnosis)
- TT Antidens
  - RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
    - (protein and DNA sequence of \*\*\*Mycobacterium\*\*\* johnei antigens

```
able to induce interferon and uses in diagnosis)
ΙT
     Interferons
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL
     (Biological study); USES (Uses)
        (.gamma., detection of, in cell supernatant; protein and DNA sequence
            ***Mycobacterium*** johnei antigens able to induce interferon
        and uses in diagnosis)
     849989-44-2 849989-47-5
TT
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP
     (Properties); BIOL (Biological study); USES (Uses)
        (amino acid sequence; protein and DNA sequence of
                                                           ***Mycobacterium***
        johnei antigens able to induce interferon and uses in diagnosis)
     849989-45-3 849989-46-4
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
                                                          ***Mycobacterium***
        (nucleotide sequence; protein and DNA sequence of
```

- johnei antigens able to induce interferon and uses in diagnosis)

  L4 ANSWER 8 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 5
- AN 2005:337763 BIOSIS <<LOGINID::20080325>>
- DN PREV200510123867
- TI Expression cloning of gamma interferon-inducing antigens of \*\*\*Mycobacterium\*\*\* avium subsp paratuberculosis.
- AU Nagata, Reiko [Reprint Author]; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Yokomizo, Yuichi; \*\*\*Mori, Yasuyuki\*\*\*
- CS Natl Inst Anim Hlth, Immune Syst Sect, Dept Immunol, 3-1-5 Kannondai, Tsukuba, Ibaraki 3050856, Japan kikuma@affrc.qo.jp
- SO Infection and Immunity, (JUN 2005) Vol. 73, No. 6, pp. 3778-3782. CODEN: INFIBR. ISSN: 0019-9567.
- DT Article
- LA English
- OS GenBank-AX094821; EMBL-AX094821; DDJB-AX094821; GenBank-U18263; EMBL-U18263; DDJB-U18263
- ED Entered STN: 31 Aug 2005
  - Last Updated on STN: 31 Aug 2005
- AB Three recombinant proteins, Map10, Map39, and Map41, produced based on nucleotide sequences obtained from the screening of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis genomic library expressed in Escherichia coli significantly elicited gamma interferon production in peripheral blood mononuclear cells from infected cattle. Two of these proteins were members of the PPE protein family.
- Expression cloning of gamma interferon-inducing antigens of \*\*\*Mycobacterium\*\*\* avium subsp paratuberculosis.
- AU Nagata, Reiko [Reprint Author]; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Yokomizo, Yuichi; \*\*\*Mori, Yasuyuki\*\*\*
- AB Three recombinant proteins, Map10, Map39, and Map41, produced based on nucleotide sequences obtained from the screening of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis genomic library expressed in Escherichia coli significantly elicited gamma interferon production in peripheral blood mononuclear cells from.
- ORGN . . . . Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms Organism Name

Escherichia coli (species): expression system Taxa Notes

Bacteria, Eubacteria, Microorganisms ORGN Classifier

\*\*\*Mycobacteriaceae\*\*\*
Super Taxa

\*\*\*Mvcobacteria\*\*\* ; Actinomycetes and Related Organisms;

Eubacteria; Bacteria; Microorganisms

Organism Name

 $$^{***}\mbox{Mycobacterium}^{***}$$  avium paratuberculosis (subspecies): pathogen Taxa Notes

08881

Bacteria, Eubacteria, Microorganisms

- L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2004:175700 CAPLUS <<LOGINID::20080325>>
- DN 140:230513
- TI Primer sets for detection of \*\*\*Mycobacterium\*\*\* avium and their uses for diagnosis of Johne's disease
- IN Kageyama, Soichi; Sawai, Takeshi; Hinosawa, Masaki; Onoe, Sadao; Watanabe, Kelko; \*\*\*Mori, Yasuyuki\*\*\*; Yoshihara, Kazuhiro; Muneta, Yoshihiro; Yokomizo, Yuichi
- PA Hokkaido Prefecture, Japan; Eiken Chemical Co., Ltd.; Nogyo Gijutsu Kenkyu Kiko
- SO Jpn. Kokai Tokkyo Koho, 34 pp.
- CODEN: JKXXAF
- DT Patent
- LA Japanese
- FAN.CNT 1

	PA:	TENT NO.	KIND	DATE	APPLICATION NO.	DATE		
PI	JP	2004065244	A	20040304	JP 2003-159573	20030604		
PRAI	JP	2002-168696	A	20020610				

- AB This invention provides primer sets for detection of \*\*\*Mycobacterium\*\*\*
  avium Paratuberculosis. The primers were used for amplification of
  \*\*\*Mycobacterium\*\*\* insertion sequence IS900. The method of detection
  of \*\*\*Mycobacterium\*\*\* can be used for diagnosis of Johne's disease.
- TI Primer sets for detection of \*\*\*Mycobacterium\*\*\* avium and their uses for diagnosis of Johne's disease
  IN Kagevama, Soichi; Sawai, Takeshi; Hinosawa, Masaki; Once, Sadao; Watanabe,
- IN Kageyama, Soichi; Sawai, Takeshi; Hinosawa, Masaki; Onoe, Sadao; Watanabe, Keiko; \*\*\*Mori, Yasuyuki\*\*\*; Yoshihara, Kazuhiro; Muneta, Yoshihiro; Yokomizo, Yuichi
- AB This invention provides primer sets for detection of \*\*\*Mycobacterium\*\*\* avium Paratuberculosis. The primers were used for amplification of \*\*\*Mycobacterium\*\*\* insertion sequence IS900. The method of detection
  - of \*\*\*Mycobacterium\*\*\* can be used for diagnosis of Johne's disease.

    I primer set detection \*\*\*Mycobacterium\*\*\* diagnosis Johne disease
- IT Insertion sequence
  - RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
    - (IS900, amplification of; primer sets for detection of
    - \*\*\*Mycobacterium\*\*\* avium and their uses for diagnosis of Johne's disease)
- IT Genetic methods
  - (LAMP, for detection of \*\*\*Mycobacterium\*\*\*; primer sets for detection of \*\*\*Mycobacterium\*\*\* avium and their uses for diagnosis of Johne's disease)

```
IT Genetic methods
        (for detection of ***Mycobacterium*** ; primer sets for detection of
         ***Mycobacterium*** avium and their uses for diagnosis of Johne's
       disease)
    Primers (nucleic acid)
    RL: BUU (Biological use, unclassified); DGN (Diagnostic use); PRP
    (Properties); BIOL (Biological study); USES (Uses)
        (for detection of ***Mycobacterium***; primer sets for detection of ***Mycobacterium*** avium and their uses for diagnosis of Johne's
       disease)
тт
    Diagnosis
       (mol., of johne's diseases; primer sets for detection of
         ***Mycobacterium*** avium and their uses for diagnosis of Johne's
TТ
    Infection
        (paratuberculosis, diagnosis of; primer sets for detection of
          ***Mycobacterium*** avium and their uses for diagnosis of Johne's
       disease)
IT 668513-71-1 668513-72-2 668513-73-3 668513-74-4 668513-75-5
    668513-76-6 668513-77-7 668513-78-8 668513-79-9 668513-80-2
    668513-81-3 668513-82-4 668513-83-5 668513-84-6 668513-85-7
    668513-86-8 668513-87-9 668513-88-0 668513-89-1 668513-90-4
    668513-91-5
                 668513-92-6
    RL: BUU (Biological use, unclassified); DGN (Diagnostic use); PRP
    (Properties); BIOL (Biological study); USES (Uses)
        (nucleotide sequence; primer sets for detection of
         ***Mycobacterium*** avium and their uses for diagnosis of Johne's
       disease)
                 668757-92-4 668757-93-5 668757-94-6 668757-95-7
ΙT
   668757-91-3
    668757-96-8 668757-97-9 668757-98-0 668757-99-1 668758-00-7
    668758-01-8 668758-02-9
    RL: PRP (Properties)
        (unclaimed nucleotide sequence; primer sets for detection of
         ***Mycobacterium*** avium and their uses for diagnosis of Johne's
       disease)
    ANSWER 10 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
L4
                                                       DUPLICATE 6
AN
    2004:438665 BIOSIS <<LOGINID::20080325>>
DN
    PREV200400437489
TT
    Neutralization of interleukin-10 significantly enhances gamma interferon
    expression in peripheral blood by stimulation with Johnin purified protein
    derivative and by infection with ***Mycobacterium*** avium subsp.
    paratuberculosis in experimentally infected cattle with paratuberculosis.
AU
    Buza, Jorann J.; Hikono, Hirokazu; ***Mori, Yasuyuki***; Nagata,
    Reiko; Hirayama, Sachiyo; Bari, Abusaleh M.; Aodon-geril; Shu, Yujing;
    Tsuji, Noriko M.; Momotani, Eiichi [Reprint Author]
    ParaTB and Inflammatory Bowel Dis Res Team, NIAH, 3-1-5 Kannondai,
    Tsukuba, Ibaraki, 3050856, Japan
    momotani@affrc.go.ip
    Infection and Immunity, (April 2004) Vol. 72, No. 4, pp. 2425-2428. print.
    ISSN: 0019-9567 (ISSN print).
    Article
DT
LA
    English
   Entered STN: 17 Nov 2004
ED
    Last Updated on STN: 17 Nov 2004
   Monoclonal antibody neutralization of interleukin-10 (IL-10) increased
```

```
Johnin purified protein derivative-induced whole-blood gamma interferon (IFN-gamma) secretion 23-fold and also increased IFN-gamma secretion ninefold following in vitro "**tMycobacterium*** avium subsp. paratuberculosis infection of peripheral blood mononuclear cells. These results demonstrate the suppressive effect of IL-10 on immune responses to M. avium subsp. paratuberculosis infection in cattle.
```

- TI. . . interleukin-10 significantly enhances gamma interferon expression in peripheral blood by stimulation with Johnin purified protein derivative and by infection with \*\*\*Mycobacterium\*\*\* avium subsp.
- paratuberculosis in experimentally infected cattle with paratuberculosis.

  AU Buza, Jorarn J.; Hikono, Hirokazu; \*\*\*Mori, Yasuyuki\*\*\*; Nagata,
  Reiko; Hirayama, Sachiyo; Bari, Abusaleh M.; Aodon-geril; Shu, Yujing;
  Tsuji, Noriko M.; Momotani, Eiichi (Reprint Author)
- AB. . . increased Johnin purified protein derivative-induced whole-blood gamma interferon (IFN-gamma) secretion 23-fold and also increased IFN-gamma secretion ninefold following in vitro \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis infection of peripheral blood mononuclear cells. These results demonstrate the suppressive effect of IL-10 on immune responses.

## ORGN . . .

Animalia Organism Name

cattle (common): immune responses

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

ORGN Classifier

\*\*\*Mycobacteriaceae\*\*\* 08881

Super Taxa

\*\*\*Mycobacteria\*\*\* ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms

Organism Name

\*\*\*Mycobacterium\*\*\* avium paratuberculosis (subspecies)

Taxa Notes

Bacteria, Eubacteria, Microorganisms

- L4 ANSWER 11 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
  - AN 2005:45686 BIOSIS <<LOGINID::20080325>>
  - DN PREV200500044914
  - TI Generation of multinucleated giant cells in vitro from bovine monocytes and macrophages.
- AU Yoshihara, Kazuhiro [Reprint Author]; Nagata, Reiko; Muneta, Yoshihiro; Inumaru, Shigeki; Yokomizo, Yuichi; \*\*\*Mori, Yasuyuki\*\*\*
  CS Natl Inst Anim Hlth, 3-1-5 Kannondai, Tsukuba, Ibaraki, 3050856, Japan
- CS Natl Inst Anim Hith, 3-1-5 Kannondai, Tsukuba, Ibaraki, 3050856, Japan SJ Journal of Veterinary Medical Science, (September 2004) Vol. 66, No. 9, pp. 1065-1069. print.

ISSN: 0916-7250 (ISSN print).

- DT Article
- LA English
- ED Entered STN: 26 Jan 2005
  - Last Updated on STN: 26 Jan 2005
- AB The generation of multinucleated giant cells (MGC) from cells of the bovine monocyte-macrophage lineage was investigated. Freshly isolated monocytes were incubated with the conditioned medium (CM) of peripheral blood mononuclear cell cultures treated with Concanavalin A for 1-4 days (CM1 to CM4). Only CM1 generated MGC despite similar concentrations of

IFNgamma in all CMs. Nevertheless, MGC formation from monocytes was enhanced by adding either macrophage colony-stimulating factor (M-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF), MGC formations from macrophages were observed only when macrophages were cultured with GM-CSF plus CM. These results indicate that several mechanisms to generate MGC from bovine monocytes-macrophage lineage cells exist, and that GM-CSF is a major mediator of MGC formation in cattle. Yoshihara, Kazuhiro [Reprint Author]; Nagata, Reiko; Muneta, Yoshihiro; Inumaru, Shiqeki; Yokomizo, Yuichi; \*\*\*Mori, Yasuyuki\*\*\* ORGN . . . Chordata; Animalia Organism Name cattle (common): host Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

ORGN Classifier

\*\*\*Mycobacteriaceae\*\*\* 08881

Super Taxa

\*\*\*Mvcobacteria\*\*\* ; Actinomycetes and Related Organisms;

Eubacteria; Bacteria; Microorganisms

Organism Name

\*\*\*Mycobacterium\*\*\* avium paratuberculosis (subspecies): pathogen Taxa Notes

Bacteria, Eubacteria, Microorganisms

- L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
- 2004:885718 CAPLUS <<LOGINID::20080325>> AN
- DN 141:363746
- TT Development of early-stage diagnostic method for Johne disease by using anti-IL-10 antibody
- AII \*\*\*Mori, Yasuyuki\*\*\* Momotani, Eiichi;
- CS Natl. Agric. Bio-oriented Res. Org., Natl. Inst. Animal Health, Tsukuba, 305-0856, Japan
- SO BRAIN Techno News (2004), 105, 18-24 CODEN: BTEEEC; ISSN: 1345-5958
- Nogvo, Seibutsukei Tokutei Sangvo Gijutsu Kenkvu Kiko, Seibutsukei Tokutei PB Sangyo Gijutsu Kenkyu Shien Senta
- DT Journal; General Review
- LA Japanese
- AB A review on early-stage diagnosis of Johne's disease (paratuberculosis) in cattle by modified interferon .gamma. ELISA assay using IL-10 neutralizing antibody, and its effectiveness.
- AU Momotani, Eiichi; \*\*\*Mori, Yasuvuki\*\*\*
- TT Bos taurus

\*\*\*Mycobacterium\*\*\* avium paratuberculosis (early-stage diagnosis method for Johne's disease using anti-IL-10 antibody)

- L4 ANSWER 13 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on DUPLICATE 7
- AN 2004:64047 BIOSIS <<LOGINID::20080325>>
- DN PREV200400065534
- \*\*\*Mvcobacterium\*\*\* avium subsp. paratuberculosis infection causes suppression of RANTES, monocyte chemoattractant protein 1, and tumor necrosis factor alpha expression in peripheral blood of experimentally infected cattle.

- AU Buza, Joram J.; \*\*\*Mori, Yasuyuki\*\*\* ; Bari, Abusaleh M.; Hikono, Hirokazu; Aodon-geril; Hirayama, Sachiyo; Shu, Yujing; Momotani, Eiichi [Reprint Author]
- CS Paratuberculosis and Inflammatory Bowel Disease Research Team, NIAH, 3-1-5 Kan-nondai, Tsukuba, 305-0856, Japan momotani@affrc.go.jp
- SO Infection and Immunity, (December 2003) Vol. 71, No. 12, pp. 7223-7227. print.
  - ISSN: 0019-9567 (ISSN print).
- DT Article
- LA English
- ED Entered STN: 28 Jan 2004
- Last Updated on STN: 28 Jan 2004
- AB Blood from cattle with subclinical \*\*\*Mycobacterium\*\*\* avium subsp.
  paratuberculosis infection was stimulated with M. avium subsp.

paratuberculosis antigens, and expression of interleukin-lbeta (IL-lbeta), tumor necrosis factor alpha (TNF-alpha), RANTES, monocyte chemoattractant protein 1 (MCP-1), and IL-8 was measured. Expression of TNF-alpha, RANTES, and MCP-1 was lower in infected than in uninfected cattle. The reduced response may weaken protective immunity and perpetuate infection.

- TI \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis infection causes suppression of RANTES, monocyte chemoattractant protein 1, and tumor necrosis factor albae expression in peripheral.
- AU Buza, Joram J.; \*\*\*Mori, Yasuyuki\*\*\* ; Bari, Abusaleh M.; Hikono, Hirokazu; Aodon-geril; Hirayama, Sachiyo; Shu, Yujing; Momotani, Eiichi [Reprint Author]
- AB Blood from cattle with subclinical \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis infection was stimulated with M. avium subsp. paratuberculosis antigens, and expression of interleukin-lbeta (IL-lbeta), tumor necrosis factor.

  ORGN .

## Animalia

Organism Name

cattle (common): host, breed-Holstein

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

ORGN Classifier

\*\*\*Mycobacteriaceae\*\*\* 08881

Super Taxa

\*\*\*Mycobacteria\*\*\* ; Actinomycetes and Related Organisms;

Eubacteria; Bacteria; Microorganisms Organism Name

\*\*\*Mycobacterium\*\*\* avium paratuberculosis (subspecies): pathogen Taxa Notes

Bacteria, Eubacteria, Microorganisms

- ANSWER 14 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2003:399194 CAPLUS <<LOGINID::20080325>>
- DN 140:39839
- TI Studies on diagnostic methods for bovine paratuberculosis
- AU \*\*\*Mori, Yasuyuki\*\*\*; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Hikono, Hirokazu; Momotani, Eiichi
- CS Immune System Section, Department of Immunology, National Institute of Animal Health, Tsukuba, 305-0856, Japan
- SO Dobutsu Eisei Kenkyusho Kenkyu Hokoku (2003), Volume Date 2002, 109, 33-42 CODEN: DEKKC9; ISSN: 1347-2542

- PB Nogyo Gijutsu Kenkyu Kiko Dobutsu Eisei Kenkyusho
- DT Journal
- LA Japanese
  - Current diagnostic tests for paratuberculosis principally rest on serol. assay, bacterial culture and the johnin skin test. However, diagnostic tests that are both sensitive and specific for detecting all subclinically affected animals have not yet been found. Therefore, a no. of studies have been conducted in order to find rapid and accurate diagnostic methods for paratuberculosis. As a result, the following have been found. (1) PCR test with internal control DNA is accurate, sensitive and rapid for the detection of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in fecal samples. (2) In the interferon gamma (IFN-.gamma.) assay using johnin purified protein deriv. (J-PPD), bovine tuberculin PPD and Con A (Con A), IFN-.gamma. responses against J-PPD were the highest in affected animals. On the contrary those of Con A were the highest in healthy animals. Interpretation of the IFN-.gamma. assay by the higher IFN-.gamma. responses against J-PPD than those of Con A is preferable as one of the diagnostic criteria. (3) Monoclonal antibody (711-1-1) which recognizes the lipoarabinomannan antigen of M. avium subsp. paratuberculosis did not react with M. avium subsp. avium, and showed potential usefulness in the serol. tests. (4) A recombinant alkyl hydroperoxide reductase C of M. avium subsp. paratuberculosis has been prepd. and successfully applied to induce IFN-.gamma. from peripheral blood mononuclear cells of animals infected with M. avium subsp. paratuberculosis. (5) In the course of study on the role of cytokines, monocyte chemoattractant protein-1 seems to be involved in the
- AU \*\*\*Mori, Yasuyuki\*\*\* ; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Hikono, Hirokazu; Momotani, Eiichi
- AB . . . following have been found. (1) PCR test with internal control DNA is accurate, sensitive and rapid for the detection of
- \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in fecal samples.
- In the interferon gamma (IFN-.gamma.) assay using johnin purified protein deriv. (J-PPD), bovine. . .
- ST cattle \*\*\*Mycobacterium\*\*\* paratuberculosis infection surface antigen
  IFN induction test; alkyl hydroperoxide reductase antigen cattle IFN
  induction \*\*\*Mycobacterium\*\*\*; reverse transcription PCR monocyte
  chemoattractant protein mRNA assav
- IT Bos taurus
  - Infection
    - \*\*\*Mycobacterium\*\*\* avium paratuberculosis (studies on diagnostic methods for bovine paratuberculosis)
- L4 ANSWER 15 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
- AN 2003:329566 BIOSIS <<LOGINID::20080325>>

pathogenesis of paratuberculosis.

- DN PREV200300329566
- TI Studies on the diagnostic methods for bovine paratuberculosis.
- AU \*\*\*Mori, Yasuyuki\*\*\* [Reprint Author]; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Hikono, Hirokazu; Momotani, Eiichi
- CS Immune System Section, Department of Immunology, National Institute of Animal Health, 3-1-5 Kannondai, Tsukuba, Ibaraki, 305-0856, Japan vamoriBaffrc.oc. ip
- SO Bulletin of the National Institute of Animal Health, (2002) No. 109, pp. 33-42. print. ISSN: 1347-2542 (ISSN print).

LA Japanese

ED Entered STN: 16 Jul 2003

Last Updated on STN: 16 Jul 2003

AR Current diagnostic tests for paratuberculosis principally rest on serological assay, bacterial culture and the johnin skin test. However, diagnostic tests that are both sensitive and specific for detecting all subclinically affected animals have not yet been found. Therefore, a number of studies have been conducted in order to find rapid and accurate diagnostic methods for paratuberculosis. As a result, the following have been found; 1) PCR test with internal control DNA is accurate, sensitive and rapid for the detection of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in faecal samples. 2) In the interferon gamma (IFN-gamma) assay using johnin purified protein derivative (J-PPD), bovine tuberculin PPD and concanavalin A (Con A), IFN-gamma responses against J-PPD were the highest in affected animals. On the contrary those of Con A were the highest in healthy animals. Interpretation of the IFN-gamma assay by the higher IFN-gamma responses against J-PPD than those of Con A is preferable as one of the diagnostic criteria. 3) Monoclonal antibody (711-1-1) which recognizes the lipoarabinomannan antigen of M. avium subsp. paratuberculosis did not react with M. avium subsp. avium, and showed potential usefulness in the serological tests. 4) A recombinant alkyl hydroperoxide reductase C of M. avium subsp. paratuberculosis has been prepared and successfully applied to induce IFN-gamma from peripheral blood mononuclear cells of animals infected with M. avium subsp. paratuberculosis. 5) In the course of study on the role of cytokines, monocyte chemoattractant protein-1 seems to be involved in the pathogenesis of paratuberculosis.

AU \*\*\*Mori, Yasuyuki\*\*\* [Reprint Author]; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; Hikono, Hirokazu; Momotani, Eiichi

AB. . following have been found; 1) PCR test with internal control DNN is accurate, sensitive and rapid for the detection of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in faecal samples. 2) In the interferon gamma (IFN-gamma) assay using johnin purified protein derivative (J-PPD), bovine. .

ORGN . . . Chordata; Animalia

Organism Name

bovine (common): host

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

ORGN Classifier

\*\*\*Mycobacteriaceae\*\*\* 08881

Super Taxa

\*\*\*Mycobacteria\*\*\* ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms

Organism Name

\*\*\*Mycobacterium\*\*\* avium paratuberculosis (subspecies): pathogen, strain-ATCC 19698, strain-Kag-1

Taxa Notes

Bacteria, Eubacteria, Microorganisms

=> e hikono hirokazu/au

E1 1 HIKONO ATSUSHI/AU

E2 26 HIKONO H/AU

```
E3
          39 --> HIKONO HIROKAZU/AU
           2 HIKONO KOICHI/AU
E4
E5
           1
                 HIKONO M/AU
           1
                HIKONO MASAHARU/AU
E6
E7
           1
                HIKONO MASAJI/AU
E8
           5
                HIKONO TAKIO/AU
E9
           1
                HIKONOV V A/AU
E10
          21
                HIKOSAKA A/AU
E11
           7
                HIKOSAKA AIZO/AU
E12
           14
                HIKOSAKA AKIHIDE/AU
=> s e2-e3 and mycobact?
          13 ("HIKONO H"/AU OR "HIKONO HIROKAZU"/AU) AND MYCOBACT?
=> dup rem 15
PROCESSING COMPLETED FOR L5
             5 DUP REM L5 (8 DUPLICATES REMOVED)
=> d bib ab kwic
    ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN
    142:334896
DN
    Method for diagnosing johne's disease
   Momotani, Eiichi; Mori, Yasuyuki; ***Hikono, Hirokazu*** ; Buza, Joram
    Josephat
   Incorporated Administrative Agency National Agriculture and Bio-Oriented
    Research Organization, Japan
SO
   PCT Int. Appl., 38 pp.
    CODEN: PIXXD2
    Patent
T.A
    Japanese
FAN.CNT 1
                     KIND DATE APPLICATION NO. DATE
    PATENT NO.
    WO 2005029079
                            20050331 WO 2003-JP11845
                                                             20030917
PT
                       A1
        W: AU, JP, US
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
            IT, LU, MC, NL, PT, RO, SE, SI, SK, TR
    AU 2003272880 A1 20050411 AU 2003-272880
                                                              20030917
    US 2008038758
                       A1
                             20080214
                                      US 2007-572514
                                                              20070426
PRAI WO 2003-JP11845
                       A
                              20030917
    A method for diagnosing johne's disease is provided, with which an animal
    infected with ***Mycobacterium*** paratuberculosis (Johne's) can be
    diagnosed at a high sensitivity in the inapparent infection stage before
    the specific antibody level begins to increase, and a large no. of
    specimens can be treated. The method is characterized in that it
    comprises collecting a blood sample of a subject animal, adding an
    anti-IL-10 antibody and a ***Mycobacterium*** paratuberculosis antigen
    to the collected blood followed by culturing, and then, measuring the
    IFN.gamma. yield in the cultured blood. The method is also characterized
    in that the IFN.gamma. yield in blood is measured by the IFN.gamma. ELISA
    method. Also provided is a method for diagnosing ***mycobacteriosis***
    , which is characterized by comprising collecting a blood sample of a
```

subject animal, adding an anti-IL-10 antibody and a \*\*\*Mycobacterium\*\*\* antigen to the collected blood followed by culturing, and then, measuring

the IFN.gamma, vield in the cultured blood.

- RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- IN Momotani, Eiichi; Mori, Yasuyuki; \*\*\*Hikono, Hirokazu\*\*\* ; Buza, Joram Josephat
- AB A method for diagnosing johne's disease is provided, with which an animal infected with \*\*\*Mycobacterium\*\*\* paratuberculosis (Johne's) can be diagnosed at a high sensitivity in the inapparent infection stage before the specific antibody level begins. . . is characterized in that it comprises collecting a blood sample of a subject animal, adding an anti-II-10 antibody and a \*\*\*Mycobacterium\*\*\* paratuberculosis antige to the collected blood followed by culturing, and then, measuring the IFN.gamma. yield in the cultured blood. The. . . that the IFN.gamma yield in blood is measured by the IFN.gamma ELISA method. Also provided is a method for diagnosing \*\*\*mycobacteriosis\*\*\*, which is characterized by comprising collecting a blood sample of a subject animal, adding an anti-II-10 antibody and a \*\*\*Mycobacterium\*\*\* antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma. yield in the cultured blood.
- IT Animals

Blood analysis

Diagnosis

\*\*\*Mycobacterium\*\*\* avium paratuberculosis

(method for diagnosing johne's disease by measuring blood IFN.gamma. by  $\mathtt{ELISA})$ 

=> d bib ab kwic 2-

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

- L6 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 1
- AN 2004:438665 BIOSIS <<LOGINID::20080325>>
- DN PREV200400437489
- TI Neutralization of interleukin-10 significantly enhances gamma interferon expression in peripheral blood by stimulation with Johnin purified protein derivative and by infection with \*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in experimentally infected cattle with paratuberculosis.
- AU Buza, Jorarn J.; \*\*\*Hikono, Hirokazu\*\*\*; Mori, Yasuyuki, Nagata, Reiko; Hirayama, Sachiyo; Bari, Abusaleh M.; Aodon-geril; Shu, Yujing; Tsuji, Noriko M.; Momotani, Eiichi [Reprint Author]
- CS ParaTB and Inflammatory Bowel Dis Res Team, NIAH, 3-1-5 Kannondai, Tsukuba, Ibaraki, 3050856, Japan momotani@affrc.go.jp
  - O Infection and Immunity, (April 2004) Vol. 72, No. 4, pp. 2425-2428. print. ISSN: 0019-9567 (ISSN print).
- DT Article
- LA English
- ED Entered STN: 17 Nov 2004
- Last Updated on STN: 17 Nov 2004
- AB Monoclonal antibody neutralization of interleukin-10 (IL-10) increased Johnin purified protein derivative-induced whole-blood gamma interferon (IFN-gamma) secretion 23-fold and also increased IFN-gamma secretion ninefold following in vitro "\*Mycobacterium"\* avium subsp. paratuberculosis infection of peripheral blood mononuclear cells. These results demonstrate the suppressive effect of IL-10 on immune responses to M. avium subsp. paratuberculosis infection in cattle.
- TI. . . interleukin-10 significantly enhances gamma interferon expression in

```
peripheral blood by stimulation with Johnin purified protein derivative
    and by infection with ***Mycobacterium*** avium subsp.
     paratuberculosis in experimentally infected cattle with paratuberculosis.
    Buza, Jorann J.; ***Hikono, Hirokazu***; Mori, Yasuyuki; Nagata,
     Reiko; Hirayama, Sachiyo; Bari, Abusaleh M.; Aodon-geril; Shu, Yujing;
     Tsuji, Noriko M.; Momotani, Eiichi [Reprint Author]
    . . increased Johnin purified protein derivative-induced whole-blood
    gamma interferon (IFN-gamma) secretion 23-fold and also increased
     IFN-gamma secretion ninefold following in vitro ***Mycobacterium***
     avium subsp. paratuberculosis infection of peripheral blood mononuclear
     cells. These results demonstrate the suppressive effect of IL-10 on
     immune responses. . .
ORGN . . .
       Animalia
     Organism Name
        cattle (common): immune responses
     Taxa Notes
        Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,
        Nonhuman Mammals, Vertebrates
ORGN Classifier
           ***Mvcobacteriaceae***
                                     08881
     Super Taxa
            ***Mycobacteria*** ; Actinomycetes and Related Organisms;
        Eubacteria; Bacteria; Microorganisms
     Organism Name
           ***Mycobacterium*** avium paratuberculosis (subspecies)
     Taxa Notes
        Bacteria, Eubacteria, Microorganisms
L6
    ANSWER 3 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
     DUPLICATE 2
    2004:64047 BIOSIS <<LOGINID::20080325>>
AN
DN
   PREV200400065534
      ***Mycobacterium*** avium subsp. paratuberculosis infection causes
TΙ
     suppression of RANTES, monocyte chemoattractant protein 1, and tumor
    necrosis factor alpha expression in peripheral blood of experimentally
     infected cattle.
    Buza, Joram J.; Mori, Yasuyuki; Bari, Abusaleh M.;
                                                        ***Hikono,***
         Hirokazu*** ; Aodon-geril; Hiravama, Sachivo; Shu, Yujing; Momotani,
     Eiichi [Reprint Author]
     Paratuberculosis and Inflammatory Bowel Disease Research Team, NIAH, 3-1-5
    Kan-nondai, Tsukuba, 305-0856, Japan
    momotani@affrc.go.ip
    Infection and Immunity, (December 2003) Vol. 71, No. 12, pp. 7223-7227.
     print.
    ISSN: 0019-9567 (ISSN print).
   Article
    English
ED
   Entered STN: 28 Jan 2004
    Last Updated on STN: 28 Jan 2004
    Blood from cattle with subclinical ***Mycobacterium*** avium subsp.
     paratuberculosis infection was stimulated with M. avium subsp.
     paratuberculosis antigens, and expression of interleukin-1beta (IL-1beta),
     tumor necrosis factor alpha (TNF-alpha), RANTES, monocyte chemoattractant
     protein 1 (MCP-1), and IL-8 was measured. Expression of TNF-alpha,
```

RANTES, and MCP-1 was lower in infected than in uninfected cattle. The reduced response may weaken protective immunity and perpetuate infection.

DТ

```
***Mycobacterium*** avium subsp. paratuberculosis infection causes
    suppression of RANTES, monocyte chemoattractant protein 1, and tumor
    necrosis factor alpha expression in peripheral. . .
    Buza, Joram J.; Mori, Yasuyuki; Bari, Abusaleh M.; ***Hikono, ***
         Hirokazu*** ; Aodon-geril; Hirayama, Sachiyo; Shu, Yujing; Momotani,
    Eiichi [Reprint Author]
    Blood from cattle with subclinical
                                        ***Mvcobacterium***
                                                             avium subsp.
    paratuberculosis infection was stimulated with M. avium subsp.
    paratuberculosis antigens, and expression of interleukin-1beta (IL-1beta),
    tumor necrosis factor. . .
ORGN . . .
       Animalia
    Organism Name
       cattle (common): host, breed-Holstein
    Taxa Notes
       Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,
       Nonhuman Mammals, Vertebrates
ORGN Classifier
           ***Mvcobacteriaceae***
                                     08881
    Super Taxa
           ***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria; Bacteria; Microorganisms
    Organism Name
           ***Mycobacterium*** avium paratuberculosis (subspecies): pathogen
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
    ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
1.6
AN
    2003:399194 CAPLUS <<LOGINID::20080325>>
DN
    140:39839
ΤТ
    Studies on diagnostic methods for bovine paratuberculosis
    Mori, Yasuyuki; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro;
AU
      ***Hikono, Hirokazu*** ; Momotani, Eiichi
    Immune System Section, Department of Immunology, National Institute of
CS
    Animal Health, Tsukuba, 305-0856, Japan
    Dobutsu Eisei Kenkyusho Kenkyu Hokoku (2003), Volume Date 2002, 109, 33-42
SO
    CODEN: DEKKC9; ISSN: 1347-2542
PB
    Nogyo Gijutsu Kenkyu Kiko Dobutsu Eisei Kenkyusho
DT
    Journal
LA
    Japanese
AB
    Current diagnostic tests for paratuberculosis principally rest on serol.
    assay, bacterial culture and the johnin skin test. However, diagnostic
    tests that are both sensitive and specific for detecting all subclinically
    affected animals have not yet been found. Therefore, a no. of studies
    have been conducted in order to find rapid and accurate diagnostic methods
    for paratuberculosis. As a result, the following have been found. (1)
    PCR test with internal control DNA is accurate, sensitive and rapid for
    the detection of ***Mycobacterium*** avium subsp. paratuberculosis in
    fecal samples. (2) In the interferon gamma (IFN-.gamma.) assay using
    johnin purified protein deriv. (J-PPD), bovine tuberculin PPD and Con A
    (Con A), IFN-.gamma. responses against J-PPD were the highest in affected
    animals. On the contrary those of Con A were the highest in healthy
    animals. Interpretation of the IFN-.gamma. assay by the higher
```

IFN-.gamma. responses against J-PPD than those of Con A is preferable as one of the diagnostic criteria. (3) Monoclonal antibody (711-1-1) which

recognizes the lipoarabinomannan antigen of M. avium subsp. paratuberculosis did not react with M. avium subsp. avium, and showed

potential usefulness in the serol. tests. (4) A recombinant alkyl hydroperoxide reductase C of M. avium subsp. paratuberculosis has been prepd. and successfully applied to induce IFN-.gamma. from peripheral blood mononuclear cells of animals infected with M. avium subsp. paratuberculosis. (5) In the course of study on the role of cytokines, monocyte chemoattractant protein-l seems to be involved in the pathogenesis of paratuberculosis.

- AU Mori, Yasuyuki; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; \*\*\*Hikono, Hirokazu\*\*\* ; Momotani, Eiichi
- AB . . . following have been found. (1) PCR test with internal control DNA is accurate, sensitive and rapid for the detection of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in fecal samples.
- (2)
  In the interferon gamma (IFN-.gamma.) assay using johnin purified protein
- deriv. (J-PPD), bovine. .
  ST cattle \*\*\*Mycobacterium\*\*\* paratuberculosis infection surface antigen
  IFN induction test; alkyl hydroperoxide reductase antigen cattle IFN
  induction \*\*\*Mycobacterium\*\*\*; reverse transcription PCR monocyte
  chemoattractant protein mRNA assay
- IT Bos taurus Infection

\*\*\*Mycobacterium\*\*\* avium paratuberculosis

(studies on diagnostic methods for bovine paratuberculosis)

- L6 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 3
- AN 2003:329566 BIOSIS <<LOGINID::20080325>>
- DN PREV200300329566
- TI Studies on the diagnostic methods for bovine paratuberculosis.
- AU Mori, Yasuyuki [Reprint Author]; Kikuma, Reiko; Muneta, Yoshihiro; Yoshihara, Kazuhiro; \*\*\*Hikono, Hirokazu\*\*\*; Momotani, Eiichi
- CS Immune System Section, Department of Immunology, National Institute of Animal Health, 3-1-5 Kannondai, Tsukuba, Ibaraki, 305-0856, Japan vamori@affrc.go.jp
- SO Bulletin of the National Institute of Animal Health, (2002) No. 109, pp. 33-42. print. ISSN: 1347-2542 (ISSN print).
- DT Article
- LA Japanese
- ED Entered STN: 16 Jul 2003
  - Last Updated on STN: 16 Jul 2003
- AB Current diagnostic tests for paratuberculosis principally rest on serological assay, bacterial culture and the johnin skin test. However, diagnostic tests that are both sensitive and specific for detecting all subclinically affected animals have not yet been found. Therefore, a number of studies have been conducted in order to find rapid and accurate diagnostic methods for paratuberculosis. As a result, the following have been found; 1) PCR test with internal control DNA is accurate, sensitive and rapid for the detection of \*\*\*Mycobacterium\*\*\* avium subsp. paratuberculosis in faecal samples. 2) In the interferon gamma (IFN-gamma) assay using johnin purified protein derivative (J-PPD), bovine tuberculin PPD and concanavalin A (Con A), IFN-gamma responses against J-PPD were the highest in affected animals. On the contrary those of Con A were the highest in healthy animals. Interpretation of the IFN-gamma assay by the higher IFN-gamma responses against J-PPD than those of Con A is preferable as one of the diagnostic criteria. 3) Monoclonal antibody (711-1-1) which recognizes the lipoarabinomannan antigen of M. avium subsp.

```
paratuberculosis did not react with M. avium subsp. avium, and showed
     potential usefulness in the serological tests. 4) A recombinant alkyl
     hydroperoxide reductase C of M. avium subsp. paratuberculosis has been
     prepared and successfully applied to induce IFN-gamma from peripheral
     blood mononuclear cells of animals infected with M. avium subsp.
    paratuberculosis. 5) In the course of study on the role of cytokines,
    monocyte chemoattractant protein-1 seems to be involved in the
     pathogenesis of paratuberculosis.
    Mori, Yasuyuki [Reprint Author]; Kikuma, Reiko; Muneta, Yoshihiro;
    Yoshihara, Kazuhiro; ***Hikono, Hirokazu***; Momotani, Eiichi
AB. . . following have been found; 1) PCR test with internal control DNA is
     accurate, sensitive and rapid for the detection of ***Mycobacterium***
     avium subsp. paratuberculosis in faecal samples. 2) In the interferon
     gamma (IFN-gamma) assay using johnin purified protein derivative (J-PPD),
     bovine. . .
ORGN . . .
       Chordata; Animalia
    Organism Name
       bovine (common): host
       Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,
       Nonhuman Mammals, Vertebrates
ORGN Classifier
           ***Mycobacteriaceae***
                                     08881
     Super Taxa
            ***Mycobacteria*** ; Actinomycetes and Related Organisms;
        Eubacteria; Bacteria; Microorganisms
     Organism Name
            ***Mycobacterium***
                               avium paratuberculosis (subspecies): pathogen,
        strain-ATCC 19698, strain-Kag-1
        Bacteria, Eubacteria, Microorganisms
=> e buza joram j/au
                BUZA J J/AU
           11
            3
                 BUZA JORAM/AU
            8 --> BUZA JORAM J/AU
            1
                 BUZA JORAM JOSEPHAT/AU
            1
                 BUZA JORARN J/AU
            4
                 BUZA K/AU
E7
           19 BUZA L/AU
                 BUZA L N/AU
            1
            1
                 BUZA L V/AU
                 BUZA LAJOSNE/AU
E10
            7
E11
            2
                 BUZA LASZLO/AU
E12
           1
                 BUZA LEJLA/AU
=> s e1-e5 and mycobact?
1.7
            11 ("BUZA J J"/AU OR "BUZA JORAM"/AU OR "BUZA JORAM J"/AU OR "BUZA
              JORAM JOSEPHAT"/AU OR "BUZA JORARN J"/AU) AND MYCOBACT?
=> dup rem 17
PROCESSING COMPLETED FOR L7
```

3 DUP REM L7 (8 DUPLICATES REMOVED)

=> d bib ab kwic 1-

E1

E2

E3

E4

E5

E6

E8

E9

YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

- ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2005:283672 CAPLUS <<LOGINID::20080325>>
- DN 142:334896
- TI Method for diagnosing johne's disease
- IN Momotani, Eiichi; Mori, Yasuyuki; Hikono, Hirokazu; \*\*\*Buza, Joram\*\*\* Josephat \*\*\*
- Incorporated Administrative Agency National Agriculture and Bio-Oriented Research Organization, Japan
- SO PCT Int. Appl., 38 pp.
- CODEN: PIXXD2
- DT Patient
- LA Japanese DAM ONT 1

FAN.CNT I																		
	PATENT NO.						D	DATE		APPLICATION NO.					DATE			
							-											
PI	WO	0 2005029079				A1		2005	0331	WO 2003-JP11845					20030917			
		W:	AU,	JP,	US													
		RW:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,
			IT,	LU,	MC,	NL,	PT,	RO,	SE,									
	ΑU	AU 2003272880						2005	0411	AU 2003-272880					20030917			
	US	2008038758				A1		2008	0214	US 2007-572514					20070426			
PRAI	WO	O 2003-JP11845				A		2003	0917									

PRAI WO 2003-JP11845

- AB A method for diagnosing johne's disease is provided, with which an animal infected with \*\*\*Mycobacterium\*\*\* paratuberculosis (Johne's) can be diagnosed at a high sensitivity in the inapparent infection stage before the specific antibody level begins to increase, and a large no. of specimens can be treated. The method is characterized in that it comprises collecting a blood sample of a subject animal, adding an anti-IL-10 antibody and a \*\*\*Mycobacterium\*\*\* paratuberculosis antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma, yield in the cultured blood. The method is also characterized in that the IFN.gamma. yield in blood is measured by the IFN.gamma. ELISA method. Also provided is a method for diagnosing \*\*\*mycobacteriosis\*\*\* , which is characterized by comprising collecting a blood sample of a subject animal, adding an anti-IL-10 antibody and a \*\*\*Mycobacterium\*\*\* antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma, vield in the cultured blood.
- THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- IN Momotani, Eiichi; Mori, Yasuyuki; Hikono, Hirokazu; \*\*\*Buza, Joram\*\*\* Josephat\*\*\*
- A method for diagnosing johne's disease is provided, with which an animal infected with \*\*\*Mycobacterium\*\*\* paratuberculosis (Johne's) can be diagnosed at a high sensitivity in the inapparent infection stage before the specific antibody level begins. . . is characterized in that it comprises collecting a blood sample of a subject animal, adding an anti-IL-10 antibody and a \*\*\*Mycobacterium\*\*\* paratuberculosis antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma. yield in the cultured blood. The. . . that the IFN.gamma. yield in blood is measured by the IFN.gamma. ELISA method. Also provided is a method for diagnosing \*\*\*mycobacteriosis\*\*\* , which is characterized by comprising collecting a blood sample of a subject animal. adding an anti-IL-10 antibody and a \*\*\*Mycobacterium\*\*\* antigen to the collected blood followed by culturing, and then, measuring the IFN.gamma. vield in the cultured blood.

```
IT Animals
    Blood analysis
    Diagnosis
        ***Mycobacterium*** avium paratuberculosis
        (method for diagnosing johne's disease by measuring blood IFN.gamma, by
       ELISA)
    ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
1.8
    DUPLICATE 1
    2004:438665 BIOSIS <<LOGINID::20080325>>
AN
DN
    PREV200400437489
    Neutralization of interleukin-10 significantly enhances gamma interferon
TI
    expression in peripheral blood by stimulation with Johnin purified protein
    derivative and by infection with ***Mycobacterium*** avium subsp.
    paratuberculosis in experimentally infected cattle with paratuberculosis.
      ***Buza, Jorarn J. *** ; Hikono, Hirokazu; Mori, Yasuyuki; Nagata,
ΑU
    Reiko; Hirayama, Sachiyo; Bari, Abusaleh M.; Aodon-geril; Shu, Yujing;
    Tsuji, Noriko M.; Momotani, Eiichi [Reprint Author]
    ParaTB and Inflammatory Bowel Dis Res Team, NIAH, 3-1-5 Kannondai,
    Tsukuba, Ibaraki, 3050856, Japan
    momotani@affrc.go.jp
    Infection and Immunity, (April 2004) Vol. 72, No. 4, pp. 2425-2428. print.
SO
    ISSN: 0019-9567 (ISSN print).
    Article
T.A
    English
ED
    Entered STN: 17 Nov 2004
    Last Updated on STN: 17 Nov 2004
    Monoclonal antibody neutralization of interleukin-10 (IL-10) increased
    Johnin purified protein derivative-induced whole-blood gamma interferon
    (IFN-gamma) secretion 23-fold and also increased IFN-gamma secretion
    ninefold following in vitro ***Mycobacterium*** avium subsp.
    paratuberculosis infection of peripheral blood mononuclear cells. These
    results demonstrate the suppressive effect of IL-10 on immune responses to
    M. avium subsp. paratuberculosis infection in cattle.
    . . interleukin-10 significantly enhances gamma interferon expression in
TI.
    peripheral blood by stimulation with Johnin purified protein derivative
    and by infection with ***Mycobacterium*** avium subsp.
    paratuberculosis in experimentally infected cattle with paratuberculosis.
AII
      ***Buza, Jorarn J. *** ; Hikono, Hirokazu; Mori, Yasuyuki; Nagata,
    Reiko; Hirayama, Sachiyo; Bari, Abusaleh M.; Aodon-geril; Shu, Yujing;
    Tsuji, Noriko M.; Momotani,.
    . . increased Johnin purified protein derivative-induced whole-blood
    gamma interferon (IFN-gamma) secretion 23-fold and also increased
    IFN-gamma secretion ninefold following in vitro ***Mycobacterium***
    avium subsp. paratuberculosis infection of peripheral blood mononuclear
    cells. These results demonstrate the suppressive effect of IL-10 on
    immune responses. .
ORGN . . .
       Animalia
    Organism Name
       cattle (common): immune responses
    Taxa Notes
       Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,
       Nonhuman Mammals, Vertebrates
ORGN Classifier
           ***Mycobacteriaceae*** 08881
    Super Taxa
```

```
***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria; Bacteria; Microorganisms
    Organism Name
           ***Mycobacterium*** avium paratuberculosis (subspecies)
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
    ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
1.8
    DUPLICATE 2
    2004:64047 BIOSIS <<LOGINID::20080325>>
DN
    PREV200400065534
      ***Mycobacterium***
                           avium subsp. paratuberculosis infection causes
    suppression of RANTES, monocyte chemoattractant protein 1, and tumor
    necrosis factor alpha expression in peripheral blood of experimentally
    infected cattle.
      ***Buza, Joram J. *** ; Mori, Yasuyuki; Bari, Abusaleh M.; Hikono,
    Hirokazu; Aodon-geril; Hirayama, Sachiyo; Shu, Yujing; Momotani, Eiichi
    [Reprint Author]
CS
   Paratuberculosis and Inflammatory Bowel Disease Research Team, NIAH, 3-1-5
    Kan-nondai, Tsukuba, 305-0856, Japan
    momotani@affrc.go.jp
    Infection and Immunity, (December 2003) Vol. 71, No. 12, pp. 7223-7227.
SO
    print.
    ISSN: 0019-9567 (ISSN print).
    Article
T.A
    English
ED
   Entered STN: 28 Jan 2004
    Last Updated on STN: 28 Jan 2004
AB
    Blood from cattle with subclinical
                                        ***Mycobacterium*** avium subsp.
    paratuberculosis infection was stimulated with M. avium subsp.
    paratuberculosis antigens, and expression of interleukin-1beta (IL-1beta),
    tumor necrosis factor alpha (TNF-alpha), RANTES, monocyte chemoattractant
    protein 1 (MCP-1), and IL-8 was measured. Expression of TNF-alpha,
    RANTES, and MCP-1 was lower in infected than in uninfected cattle. The
    reduced response may weaken protective immunity and perpetuate infection.
      ***Mycobacterium*** avium subsp. paratuberculosis infection causes
    suppression of RANTES, monocyte chemoattractant protein 1, and tumor
    necrosis factor alpha expression in peripheral.
      ***Buza, Joram J.*** ; Mori, Yasuyuki; Bari, Abusaleh M.; Hikono,
    Hirokazu; Aodon-geril; Hirayama, Sachiyo; Shu, Yujing; Momotani, Eiichi
    [Reprint Author]
    Blood from cattle with subclinical
                                        ***Mycobacterium***
                                                              avium subsp.
    paratuberculosis infection was stimulated with M. avium subsp.
    paratuberculosis antigens, and expression of interleukin-1beta (IL-1beta),
    tumor necrosis factor. . .
ORGN . . .
       Animalia
    Organism Name
       cattle (common): host, breed-Holstein
    Taxa Notes
       Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,
       Nonhuman Mammals, Vertebrates
ORGN Classifier
           ***Mvcobacteriaceae***
                                    08881
    Super Taxa
            ***Mycobacteria*** ; Actinomycetes and Related Organisms;
       Eubacteria; Bacteria; Microorganisms
```

AN

TI

ΑU

DT

ΤI

ΑU

AB

Organism Name \*\*\*Mycobacterium\*\*\* avium paratuberculosis (subspecies): pathogen Taxa Notes Bacteria, Eubacteria, Microorganisms => s paratuberculosis and interleukin? and interferon? and (diagnos? or assay?) 36 PARATUBERCULOSIS AND INTERLEUKIN? AND INTERFERON? AND (DIAGNOS? OR ASSAY?) => dup rem 19 PROCESSING COMPLETED FOR L9 19 DUP REM L9 (17 DUPLICATES REMOVED) => d bib ab kwic 1-YOU HAVE REQUESTED DATA FROM 19 ANSWERS - CONTINUE? Y/(N):y L10 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN AN 2007:906779 CAPLUS <<LOGINID::20080325>> DN 147:275692 TI Sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in the early stages and paucibacillary infections Ottenhof, Tom Henricus Maria; Geluk, Annemieke; Pereira Sampaio, Elizabeth Leiden University Medical Center, Neth. PCT Int. Appl., 70pp. CODEN: PIXXD2 Patent English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----------\_\_\_\_\_ ----WO 2007091881 A2 20070816 WO 2006-NL50105 20060428 WO 2007091881 A3 20071129 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

TN

PA

SO

DT

LA

PΙ

PRAI EP 2005-103576 A 20050429 The current invention discloses new Mycobacterium leprae antigens to be used in methods and means for detection and \*\*\*diagnostics\*\*\* of M. leprae infections in subjects, in particular in the early stages of infection and in paucibacillary infections, which remain undetected using conventional \*\*\*diagnostic\*\*\* methods. The antigens disclosed in the invention are specific for M. leprae and the \*\*\*diagnostic\*\*\* method does not vield 'false pos.' results in individuals having an immune response against other Mycobacterial species, such as M. tuberculosis, M. bovis, M. \*\*\*paratuberculosis\*\*\* , M. avium, M. smegmatis,, M. ulcerans, M. microti, and M. marinum, or BCG vaccinated individuals.

KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

Thus, using bioinformatic anal. the antigen genes ML0573, ML0574, ML0575, ML0576, ML1602, ML1603, ML1604, ML1788, ML1989, ML1990, ML2283 and ML2567 were found to be unique to M. leprae. It was demonstrated, that all of above genes were expressed at the mRNA level in human leprosy tissue. Paucibacillary and reactional leprosy patients and healthy household contacts of leprosy patients produced significant levels of

\*\*\*interferon\*\*\* (IPN)-.gamma. in response to the five unique M. leprae antigens encoded by ML0576, ML1989, ML1990, ML2283 and ML2567. Provided are gene and protein sequences, as well as sequences for epitope peptides for M. leprae-specific antigens ML0576, ML1989, ML1990, ML2283 and ML2567. A method for identifying Mycobacterium leprae antigens is also provided. Sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*\*idencesing\*\* Mlsprae.particularly in the early

It sequences for Mycobacterium leprae-specific antigens, and methods for treating and "\*\*diagnosing\*\*\* M. leprae, particularly in the early stages and paucibacillary infections

The outrant invention displaces new Mycobacterium leaves entigens to be a sequenced.

The current invention discloses new Mycobacterium leprae antigens to be used in methods and means for detection and \*\*\*diagnostics\*\*\* of M. leprae infections in subjects, in particular in the early stages of infection and in paucibacillary infections, which remain undetected using \*\*\*diagnostic\*\*\* methods. The antigens disclosed in the conventional invention are specific for M. leprae and the \*\*\*diagnostic\*\*\* method does not vield 'false pos.' results in individuals having an immune response against other Mycobacterial species, such as M. tuberculosis, M. bovis, M. \*\*\*paratuberculosis\*\*\* , M. avium, M. smegmatis,, M. ulcerans, M. microti, and M. marinum, or BCG vaccinated individuals. Thus, using bioinformatic anal. the. . . in human leprosy tissue. Paucibacillary and reactional leprosy patients and healthy household contacts of leprosy patients produced significant levels of \*\*\*interferon\*\*\* (IFN)-.gamma. in response to the five unique M. leprae antigens encoded by ML0576, ML1989, ML1990, ML2283 and ML2567. Provided

are. . . sequence Mycobacterium leprae antigen epitope \*\*\*diagnoses\*\*\* infection; leprosy immunodiagnosis Mycobacterium leprae antigen epitope; vaccine Mycobacterium leprae antigen epitope

IT Receptors

RL: BSU (Biological study, unclassified), BIOL (Biological study) (4-1BB, anti-4-1BB agonistic antibody as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

T Human groups

(Brazilian patients; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Genetic element

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (COPG island, COPG, as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and "\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibactilary infections)

IT Histocompatibility antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study) (HLA, class I, identifying T-cell epitopes for, using computer algorithms; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Histocompatibility antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(HLA, class II, identifying T-cell epitopes for, using computer algorithms; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) Proteins

ΙT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

> (LAG3 (lymphocyte activation gene-3), sol., as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and

paucibacillary infections)

ΙT Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML0573, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML0574, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

TΤ Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML0575, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

Gene, microbial ΙT

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML0576, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

ΙT Antigens

> RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(ML0576; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML1602, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML1603, expressed in human leprosy tissue; sequences for Mycobacterium

```
leprae-specific antigens, and methods for treating and
  ***diagnosing*** M. leprae, particularly in early stages and
  paucibacillary infections)
Gene, microbial
RI: ADV (Adverse effect, including toxicity); BSU (Biological study,
unclassified); PRP (Properties); BIOL (Biological study)
(ML1604, expressed in human leprosy tissue; sequences for Mycobacterium
leprae-specific antigens, and methods for treating and
  ***diagnosing*** M. leprae, particularly in early stages and
```

# paucibacillary infections) IT Gene, microbial

RI: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML1788, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

# IT Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRF (Properties); BIOL (Biological study) (ML1989, expressed in human lebrosy tissue; sequences for Mycobacterium

leprae-specific antigens, and methods for treating and
 \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and
paucibacillary infections)

## IT Antigens

RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(ML1989; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

#### T Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML1990, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

#### T Antigens

RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(ML1990; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

# IT Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML2283, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and

paucibacillary infections)

## IT Antigens

RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use);

PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(ML2283; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*dlagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML2567, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Antigens

RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(ML2567; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Lipopeptides

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Pam3Cys, as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Immunostimulants

(adjuvants, DA/TDB; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Immunostimulants

(adjuvants, DDA/MPL; sequences for Mycobacterium leprae-epecific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Immunostimulants
(adjuvants: se

(adjuvants, sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Monocyte

(anal., in \*\*\*diagnosis\*\*\* ; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT \*\*\*Diagnostic\*\*\* agents

Vaccines

(antigens or epitopes as; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Lipid A

Lipopolysaccharides

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Mycobacterium

(as recombinant expression host; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*dianosing\*\*\* M. leprae, particularly in early stages and

paucibacillary infections) ΙT Flagellins RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (bacterial, as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) ΙT CD40 (antigen) RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (binding CD40 ligand or antibody, as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) IΤ Mammalia ( \*\*\*diagnosis\*\*\* and therapy; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) Mycobacterium avium Mycobacterium bovis Mycobacterium marinum Mycobacterium microti Mycobacterium smegmatis Mycobacterium tuberculosis Mycobacterium ulcerans (differentiating from; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* particularly in early stages and paucibacillary infections) TT Leprosv \*\*\*diagnosis\*\*\* ; sequences for Mycobacterium (early stages leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) T cell (lymphocyte) (epitopes; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) ΙT Epitopes (from ML0576, ML1989, ML1990, ML2283 and ML2567 antigens; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) T cell (lymphocyte)

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

ΙT

Algorithm
(identifying HLA class I and/or class II T-cell epitopes using;
sequences for Mycobacterium leprae-specific antigens, and methods for
treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early
stages and pa

(helper cell, measuring response, in \*\*\*diagnosis\*\*\*; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

IT \*\*\*Diagnosis\*\*\*

(immunodiagnosis, of ML0576, ML1989, ML1990, ML2283 and ML2567 antigens; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Blood analysis

```
(in ***diagnosis*** ; sequences for Mycobacterium leprae-specific
       antigens, and methods for treating and ***diagnosing*** M. leprae,
       particularly in early stages and paucibacillary infections)
      ***Interleukin*** 10
TT
        ***Interleukin***
                           15
        ***Interleukin***
                           2
        ***Interleukin***
        ***Interleukin***
                           6
    Macrophage inflammatory protein 1.beta.
    Transforming growth factor .beta.
    Tumor necrosis factors
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); ANST (Analytical study); BIOL (Biological study)
        (measuring response, in ***diagnosis*** ; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
ΙT
    Antibodies and Immunoglobulins
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (monoclonal, anti-4-1BB, agonistic, as adjuvant; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    Genome
       (of M. leprae, identifying unique antigen gene candidates in; sequences
       for Mycobacterium leprae-specific antigens, and methods for treating
             ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
ΙT
    Protein sequences
        (of M. leprae-specific antigens ML0576, ML1989, ML1990, ML2283 and
       ML2567; sequences for Mycobacterium leprae-specific antigens, and
       methods for treating and ***diagnosing*** M. leprae, particularly
       in early stages and paucibacillary infections)
ΙT
    DNA sequences
       (of M. leprae-specific genes ML0576, ML1989, ML1990, ML2283 and ML2567;
       sequences for Mycobacterium leprae-specific antigens, and methods for
       treating and ***diagnosing*** M. leprae, particularly in early
       stages and paucibacillary infections)
ΤТ
    Blood cell
       (of infected subject, IFN-.gamma. response in; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
IΤ
       ***Interleukin*** 12
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); ANST (Analytical study); BIOL (Biological study)
        (p70, measuring response, in ***diagnosis***; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    Human
        (patients; sequences for Mycobacterium leprae-specific antigens, and
       methods for treating and ***diagnosing*** M. leprae, particularly
       in early stages and paucibacillary infections)
    Infection
        (paucibacillary,
                         ***diagnosis*** ; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
```

```
***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    Bioinformatics
       (sequence annotation, M. leprae unique genes; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
TТ
    Molecular cloning
    Mycobacterium leprae
    Test kits
       (sequences for Mycobacterium leprae-specific antigens, and methods for
       treating and ***diagnosing*** M. leprae, particularly in early
       stages and paucibacillary infections)
ΙT
    Skin
        (test, by applying antigen under top skin; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
ΙT
    Mycobacterium BCG
        (vaccine, differentiating from; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
       ***Interferons***
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); ANST (Analytical study); BIOL (Biological study)
        (.alpha., measuring response, in ***diagnosis***; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
       ***Interferons***
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); ANST (Analytical study); BIOL (Biological study)
        (.beta., measuring response, in ***diagnosis*** ; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
       ***Interferons***
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); ANST (Analytical study); BIOL (Biological study)
        (.gamma., measuring response, in ***diagnosis***; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    141256-04-4, OS21
```

particularly in early stages and paucibacillary infections) IT  $946442{-}88{-}2 \quad 946442{-}91{-}7$ 

RL: PRP (Properties) (Unclaimed; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in the early stages and paucibacillary infections)

IT 946400-78-8 946400-79-9 946400-80-2 946400-81-3 946400-82-4
RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use);

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MPL, as adjuvant; sequences for Mycobacterium leprae-specific
anticens, and methods for treating and \*\*\*diagnosinc\*\*\* M. leprae,

PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (amino acid sequence, epitope; sequences for Mycobacterium

(amino acid sequence, epitope; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT 946442-b2-0 946442-55-1 946442-54-2 946442-55-3 946442-56-4 RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(amino acid sequence; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT 24939-03-5, Poly(I:C) 87420-41-5, Pam3Cys 911642-39-2, IC 31 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

in early stages and paucibacillary infections IT 83869-56-1, GM-CSF

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (measuring response, in \*\*\*diagnosis\*\*\*; sequences for

Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT 946442-57-5, DNA (Mycobacterium leprae gene ML0576) 946442-58-6, DNA (Mycobacterium leprae gene ML1989) 946442-59-7, DNA (Mycobacterium leprae gene ML1990) 946442-60-0, DNA (Mycobacterium leprae gene ML2283) 946442-61-1, DNA (Mycobacterium leprae gene ML2283) RL: ADV (Adverse effect, including toxicity); BSU (Biological study,

unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; sequences for Mycobacterium leprae-specific
antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae,
particularly in early stages and paucibacillary infections)

IT 946442-98-4 946442-99-5 946443-00-1 946443-01-2 946443-02-3 946443-03-4 946443-04-5 946443-05-6 946443-06-7 946443-07-8 946443-08-9 946443-09-0 RJ: PRP (Properties)

(unclaimed nucleotide sequence; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in the early stages and paucibacillary infections)

IT 946442-86-0 946442-87-1 946442-89-3 946442-90-6 946442-92-8 946442-93-9 946442-94-0 946442-95-1 946442-96-2 946442-97-3 RL: PRP (Properties)

(unclaimed protein sequence; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in the early stages and paucibacillary infections)

- L10 ANSWER 2 OF 19 MEDLINE on STN
- AN 2007416292 MEDLINE <<LOGINID::20080325>>
- DN PubMed ID: 17502388
- TI Influence of Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* or colitis development and specific immune responses during disease.
- AU Singh Udai P; Singh Shailesh; Singh Rajesh; Karls Russell K; Ouinn

- Frederick D; Potter Morris E; Lillard James W Jr
- CS Brown Cancer Center, Department of Microbiology and Immunology, University of Louisville, 580 S. Preston Street, Baxter II/Room 304C, Louisville, KY 40202, USA.
- NC AI 57808 (United States NIAID)
  - GM 08248 (United States NIGMS) MD 000525 (United States NCMHD)
  - RR 03034 (United States NCRR)
- SO Infection and immunity, (2007 Aug) Vol. 75, No. 8, pp. 3722-8. Electronic Publication: 2007-05-14.
  - Journal code: 0246127, ISSN: 0019-9567,
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., EXTRAMURAL) (RESEARCH SUPPORT, NON-U.S. GOV'T)
- LA English
- FS Priority Journals
- EM 200709
- ED Entered STN: 20 Jul 2007
  - Last Updated on STN: 7 Sep 2007 Entered Medline: 6 Sep 2007
- AB The granulomatous and intramural inflammation observed in cases of inflammatory bowel diseases (IBD) and veterinary Johne's diseases suggests that Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* is a causative agent. Bowever, an incomplete understanding of the immunological steps responsible for the pathologies of IBD makes this conclusion uncertain. Sera from \*\*\*interleukin\*\*\* -10-deficient (II-10(-/-)) mice with spontaneous colitied displayed significantly higher M. avium subsp.
  - \*\*\*paratuberculosis\*\*\* -specific immunoglobulin G2a antibody responses than did sera from similar mice without disease. Pathogen-free IL-10(-/-) mice received control vehicle or the vehicle containing heat-killed or live M. avium subsp. \*\*\*paratuberculosis\*\*\*. Mucosal CD4(\*) T cells from the mice that developed colitis proliferated and secreted higher levels of gamma \*\*\*interferon\*\*\* and tumor necrosis factor alpha after ex vivo stimulation with a Vbetal1(\*) T-cell receptor-restricted peptide from the MPT59 antigen (Ag65B) than those secreted from cells from mice before the onset of colitis. The data from this study provide important information regarding the mechanisms of colitis in IL-10(-/-) mice, which are driven in part by Ag65B-specific T cells. The data suggest a plausible mechanism of Ag-specific T-cell responses in colitis driven by potent Ags conserved in Mycobacterium species.
- TI Influence of Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* or colitis development and specific immune responses during disease.
- AB . . and intramural inflammation observed in cases of inflammatory bowel diseases (IBD) and veterinary Johne's disease suggests that Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* is a causative agent. However, an incomplete understanding of the immunological steps responsible for the pathologies of IBD makes this conclusion uncertain. Sera from \*\*\*interleukin\*\*\* -10-deficient (IL-10(-/-)) mice with spontaneous colitis displayed significantly higher M. avium subsp.
  - \*\*\*paratuberculosis\*\*\* -specific immunoglobulin G2a antibody responses than did sear from similar mice without disease. Pathogen-free IL-10(-/-) mice received control vehicle or the vehicle containing heat-killed or live M. avium subsp. \*\*\*paratuberculosis\*\*\*. Mucosal CD4(+) T cells from the mice that developed colitis proliferated and secreted higher levels of gamma \*\*\*interferon\*\*\* and tumor necrosis factor alpha after ex vivo stimulation with a Vbetall(+) T-cell receptor-restricted peptide

```
from the MPT59 antigen (Ag85B). . .
    . . .
Antigens, Bacterial: IM, immunology
     CD4-Positive T-Lymphocytes: IM, immunology
     Colitis: IM, immunology
     *Colitis: MI, microbiology
     *Colitis: PA, pathology
      Disease Models, Animal
         *** Enzyme-Linked Immunosorbent Assay***
      Humans
      Immunoglobulin G: BL, blood
         *** Interferon Type II: BI, biosynthesis***
         *** Interleukin-10: DF, deficiency***
      Intestinal Mucosa: IM, immunology
      Ligands
     Mice
     Mice, Knockout
         ****Mycobacterium avium subsp. paratuberculosis: IM, immunology***
         ****Paratuberculosis: IM, immunology***
         ****Paratuberculosis: PA, pathology***
      Peptides: IM, immunology
     Receptors, Antigen, T-Cell: IM, immunology
      Receptors, CXCR3
     Receptors, Chemokine: AG, agonists
     Receptors, Chemokine: IM, immunology
      ***130068-27-8 (Interleukin-10)*** ; ***82115-62-6 (Interferon Type***
         TT) ***
CN.
    . . 0 (Peptides); 0 (Receptors, Antigen, T-Cell); 0 (Receptors, CXCR3);
     0 (Receptors, Chemokine); 0 (Tumor Necrosis Factor-alpha); 0 (antigen 85B,
    Mycobacterium
                   ***paratuberculosis*** )
L10 ANSWER 3 OF 19 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN
    2006:496945 BIOSIS <<LOGINID::20080325>>
DN
    PREV200600503265
ΤI
    Disturbed cytokine response to mycobacterium avium subspecies
      ***paratuberculosis*** is dysregulated in patients with Crohn's
disease.
     Sibartie, Shomik; Keohane, John; Scully, Paul; O'Neill, Shaun; O'Mahony,
     Jim; O'Mahony, Liam; Shanahan, Fergus
    Gastroenterology, (APR 2006) Vol. 130, No. 4, Suppl. 2, pp. A240.
    Meeting Info.: Digestive Disease Week Meeting/107th Annual Meeting of the
     American-Gastroenterological-Association. Los Angeles, CA, USA. May 19
     -24, 2006. Amer Gastroenterol Assoc Inst.
     CODEN: GASTAB. ISSN: 0016-5085.
    Conference; (Meeting)
    Conference; Abstract; (Meeting Abstract)
    English
ED
   Entered STN: 4 Oct 2006
    Last Updated on STN: 4 Oct 2006
     Background: Mycobacterium avium subspecies ***paratuberculosis***
     (MAP) has been a source of controversy since it was first suggested as a
    possible cause for Crohn's disease. While a number of studies have
     focused on identification of the organism in Crohn's disease tissues and
    others have assessed the serologic response to MAP, few studies have
    examined the cellular immune response to MAP. Aim: To compare the
     cellular response to Mycobacterium avium subspecies
```

```
***paratuberculosis*** between Crohn's disease patients and healthy
    volunteers. Methods: Peripheral blood mononuclear cells (PBMCs) were
    isolated from 24 Crohn's disease patients and 20 healthy volunteers.
    After in-vitro co-incubation for 72 his with MAP ATCC 43019 at several
    concentrations, supernatants were harvested and analysed for
    IL2, IL-4, IL-6, IL-8, IL-10, TNF-alpha and IFN-gamma using cytometric bead
    analysis. PBMCs stimulated with Salmonella typhimurium (ST)were used as
    positive controls. Results: Compared to healthy volunteers, PBMCs from
    Crohn's disease patients secreted higher levels(p < 0.05)of IL-6(4265 +/-
    260 vs. 2865 +/- 386 pg/ml), TNF-alpha (2190 +/- 247 vs. 1200 +/- 228pg/ml)
    and IL-10(265 +/- 53 vs. 81 +/- 12 pg/ml) upon exposure to MAP(1 MAP
    bacterial cell:1 PBMC) but showed no difference when exposed to ST. There
    was a lower IFN-gamma response from Crohn's disease, patients to MAP(322
    125 vs. 1658 424 pg/ml) but this also occurred in response to ST. The
    ratio of IFN-gamma to IL-10 was significantly lower for Cretin's disease
    patients' PBMCs exposed to MAP compared to healthy volunteers (p <
    0.05) but not for ST. There were no differences in IL-8, IL-2 and IL-4
    levels. Prior BCG vaccination and concurrent immunosuppressives had no
    impact on the levels of cytokines secreted. Conclusion: A diminished Th1
    response to MAP in Crohn's disease patients may allow for prolonged
    intracellular survival of MAP in phagocytic cells. This might account for
    the increased frequency of MAP detection in patients with Crohn's disease
    but does not imply cause and effect.
    Disturbed cytokine response to mycobacterium avium subspecies
      ***paratuberculosis*** is dysregulated in patients with Crohn's
disease.
    Background: Mycobacterium avium subspecies ***paratuberculosis***
    (MAP) has been a source of controversy since it was first suggested as a
    possible cause for Crohn's disease. While. . . few studies have
    examined the cellular immune response to MAP. Aim: To compare the
    cellular response to Mycobacterium avium subspecies
      ***paratuberculosis*** between Crohn's disease patients and healthy
    volunteers. Methods: Peripheral blood mononuclear cells (PBMCs) were
    isolated from 24 Crohn's disease patients.
       system, blood and lymphatics, PBMC; phagocytic cell: immune system
       Crohn's disease: digestive system disease, immune system disease,
       etiology, ***diagnosis***
    Chemicals & Biochemicals
       cvtokines; IFN-gamma [ ***interferon*** -gamma]; IL-10 [
         ***interleukin*** -10]; TNF-alpha [tumor necrosis factor-alpha]; IL-6
        [ ***interleukin*** -6]; IL-8 [ ***interleukin*** -8]; IL-2 [
         ***interleukin*** -2]; IL-4 [ ***interleukin*** -4]
ORGN . . .
       Primates, Vertebrates
ORGN Classifier
       Mycobacteriaceae 08881
    Super Taxa
       Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
       Bacteria; Microorganisms
    Organism Name
       Mycobacterium avium ***paratuberculosis*** (subspecies): pathogen
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
```

ΙT

- AN 2006:423091 BIOSIS <<LOGINID::20080325>>
- DN PREV200600423340
- TI Differential expression of genes encoding CD30L and P-selectin in cattle with Johne's disease: Progress toward a \*\*\*diagnostic\*\*\* gene expression signature.
- AU Skovgaard, Kerstin [Reprint Author]; Grell, Susanne Nedergaard; Heegaard, Peter M. H.; Jungersen, Gregers; Pudrith, Chas B.; Coussens, Paul M.
- CS Danish Inst Food and Vet Res, Dept Vet Diagnost and Res, Bulowsvej 27, DK-1790 Copenhagen V, Denmark kis@dfvf.dk
- SO Veterinary Immunology and Immunopathology, (AUG 15 2006) Vol. 112, No. 3-4, pp. 210-224.
  CODEN: VIIMOS. ISSN: 0165-2427.
- DT Article
- LA English
- ED Entered STN: 23 Aug 2006
- Last Updated on STN: 23 Aug 2006
- AB Mycobacterium avium subspecies \*\*\*paratuberculosis\*\*\* (Mycobacterium \*\*\*paratuberculosis\*\*\* ), the causative agent of \*\*\*paratuberculosis\*\*\*

(paraTB) or Johne's disease in ruminants, is a health problem for the global cattle industry with significant economic losses related to decreased milk production and reduced fertility. Commonly paraTB in cattle is \*\*\*diagnosed\*\*\* by antibody detection by serum enzyme-linked immunosorbent \*\*\*assay\*\*\* (ELISA), by detection of the pathogen by cultivation of individual faecal samples, or by in vitro measurement of cell mediated immune responses using the IFN-gamma test. There is an \*\*\*diagnostic\*\*\* approaches as all ongoing need for developing new currently available \*\*\*diagnostic\*\*\* tests for paraTB may fail to detect sub-clinical infection. We used cDNA microarrays to simultaneously measure expression of over 1300 host genes to help identify a subset of gene expression changes that might provide a unique gene expression signature for paraTB infection. In the present study, non-stimulated leukocytes isolated from 10 sub-clinical paraTB infected cows were examined for genes being expressed at significantly different levels than in similar cells from control cows with the same herd background. We included cattle (Holstein) from two locations (Denmark and USA) for the microarray experiment. Our results indicate that expression profiles of at least 52 genes are different in leukocytes from M.

 $$^{***}$  paratuberculosis  $$^{***}$$  infected cattle compared to control cattle. Gene

expression differences were verified by quantitative real-time reverse transcriptase polymerase chain reactions (QRT-PCR) on the same group of cattle (Holstein) used for the microarray experiment. In order to assess the generality of the observed gene expression, a second and different group of cattle (Jersey) was also examined using QRT-PCR. Out of the seven genes selected for QRT-PCR. CD30 ligand (CD30L) and P-selectin were consistently differentially expressed in freshly isolated leukocytes from paraTB infected and control animals of both breeds of cattle. Although further work is clearly needed to develop a more complete gene expression signature specific for paraTB, our results demonstrate that a subset of genes in leukocytes are consistently expressed at different levels, depending upon M. \*\*\*paratuberculosis\*\*\* infection status. (c) 2006

TI Differential expression of genes encoding CD30L and P-selectin in cattle with Johne's disease: Progress toward a \*\*\*diagnostic\*\*\* gene expression signature.

Elsevier B.V. All rights reserved.

AB Mycobacterium avium subspecies \*\*\*paratuberculosis\*\*\* (Mycobacterium \*\*\*paratuberculosis\*\*\* ), the causative agent of

\*\*\*paratuberculosis\*\*\*

(paraTB) or Johne's disease in ruminants, is a health problem for the global cattle industry with significant economic losses related to decreased milk production and reduced fertility. Commonly paraTB in cattle is \*\*\*diagnosed\*\*\* by antibody detection by serum enzyme-linked immunosorbent \*\*\*assav\*\*\* (ELISA), by detection of the pathogen by cultivation of individual faecal samples, or by in vitro measurement of cell mediated immune responses using the IFN-gamma test. There is an ongoing need for developing new \*\*\*diagnostic\*\*\* approaches as all currently available \*\*\*diagnostic\*\*\* tests for paraTB may fail to detect sub-clinical infection. We used cDNA microarrays to simultaneously measure expression of over 1300. . . the microarray experiment. Our results indicate that expression profiles of at least 52 genes are different in leukocytes from M. \*\*\*paratuberculosis\*\*\* infected cattle compared to control cattle. Gene expression differences were verified by quantitative real-time reverse transcriptase polymerase chain reactions (gRT-PCR). . . paraTB, our results demonstrate that a subset of genes in leukocytes are consistently expressed at different levels, depending upon M. \*\*\*paratuberculosis\*\*\* infection status. (c) 2006 Elsevier B.V. All rights reserved.

IT . . . Organisms

feces: digestive system; leukocyte: immune system, blood and lymphatics

IT Diseases Johne's disease: bacterial disease, infectious disease

IT Diseases

\*\*\*paratuberculosis\*\*\* : bacterial disease, infectious disease, etiology

\*\*\*Paratuberculosis\*\*\* (MeSH)

IT Chemicals & Biochemicals

IFN-gamma [ \*\*\*interferon\*\*\* -gamma]; cDNA [complementary DNA]
GEN. . leukemia inhibitory factor mRNA gene] (Bovidae); bovine
TNF-alpha-CE gene [bovine tumor necrosis factor-alpha-converting enzyme
gene] (Bovidae); bovine IL-IRA gene [bovine \*\*\*interleukin\*\*\* -1

gene] (Bovidae); bovine IL-1RA gene [bovine \*\*\*interleukin\*\*\* -1 receptor antagonist mRNA gene] (Bovidae); bovine P-selectin gene [bovine P-selectin mRNA gene] (Bovidae); bovine Caspase-7 gene [bovine Mch-7 isoform alpha. . .

L10 ANSWER 5 OF 19 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 1

AN 2005:498376 BIOSIS <<LOGINID::20080325>>

DN PREV200510279086

TI Bovine NK cells can produce gamma \*\*\*interferon\*\*\* in response to the secreted mycobacterial proteins ESAT-6 and MPP14 but not in response to MPB70.

AU Olsen, Ingrid [Reprint Author]; Boysen, Preben; Kulberg, Siri; Hope, Jayne C.; Jungersen, Gregers; Storset, Anne K.

CS Natl Vet Inst, POB 8156 DEP, N-0033 Oslo, Norway

Ingrid.Olsen@vetinst.no

SO Infection and Immunity, (SEP 2005) Vol. 73, No. 9, pp. 5628-5635. CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 16 Nov 2005 Last Updated on STN: 16 Nov 2005

- AB Bovine NK cells have recently been characterized and the present study describes the interaction between NK cells, antigen-presenting cells, and secreted mycobacteriall proteins. Gamma \*\*\*interferon\*\*\* (IFN-qamma) production by NK cells was seen in approximately 30% of noninfected calves in response to the Mycobacterium tuberculosis complex-specific protein ESAT-6, MPP14 from Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* and purified protein derivative (PPD) from M. tuberculosis. In contrast, no response was induced by MPB70, which is another M. tuberculosis complex-specific secreted antigen. The production of IFN-gamma by NK cells in whole blood in response to ESAT-6 and MPP14 was demonstrated using intracellular staining together with surface labeling for the NK cell-specific receptor, NKp46, or CD3. Furthermore, the depletion of NK cells from peripheral blood mommuclear cells completely abolished the IFN-gamma production. The response was mediated through stimulation of adherent cells and was largely independent of contact between adherent cells and the NK cells. Neutralization of \*\*\*interleukin\*\*\* -12 only partly inhibited IFN-gamma production, showing that other cytokines were also involved. The demonstration of NK cell-mediated IFN-gamma production in young cattle provides an explanation for the nonspecific IFN-gamma response frequently encountered in young cattle when using the IFN-gamma
- TI Bovine NK cells can produce gamma \*\*\*interferon\*\*\* in response to the secreted mycobacterial proteins ESAT-6 and MPP14 but not in response to MPB70.

test in \*\*\*diagnosis\*\*\* of mycobacteriall infections.

AB. . recently been characterized and the present study describes the interaction between NK cells, antigen-presenting cells, and secreted mycobacteriall proteins. Gamma \*\*\*interferon\*\*\* (IFN-gamma) production by NK cells was seen in approximately 30% of noninfected calves in response to the Mycobacterium tuberculosis complex-specific protein ESAT-6, NFP14 from Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\*, and purified protein derivative (PFD) from M. tuberculosis. In contrast, no response was induced by NFB70, which is another M. . . through stimulation of adherent cells and was largely independent of contact between adherent cells and the NK cells. Neutralization of \*\*\*interleukin\*\*\* -12 only partly inhibited IFN-gamma production,

showing

that other cytokines were also involved. The demonstration of NK cell-mediated IFN-gamma production in. . . cattle provides an explanation for the nonspecific IFN-gamma response frequently encountered in young cattle when using the IFN-gamma test in \*\*\*diagnosis\*\*\* of mycobacteriall infections.

IT Diseases

mycobacterial infection: bacterial disease, \*\*\*diagnosis\*\*\*

Mycobacterium Infections (MeSH)

IT Chemicals & Biochemicals

CD3; \*\*\*interferon\*\*\* -gamma [IFN-gamma]; \*\*\*interleukin\*\*\* -12; ESAT-6; NKp46; purified protein derivative; MPB70; mycobacterial proteins; MPP14

ORGN . . .

Classifier

Mycobacteriaceae 08881

Super Taxa

Mycobacteria; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms

```
Organism Name
       Mycobacterium tuberculosis (species): pathogen
       Mycobacterium avium ***paratuberculosis*** (subspecies): pathogen
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
L10 ANSWER 6 OF 19
                       MEDLINE on STN
    2005487701
                 MEDLINE <<LOGINID::20080325>>
    PubMed ID: 15992970
    Vaccination of sheep against M. ***paratuberculosis*** : immune
    parameters and protective efficacy.
    Beag D J; Griffin J F T
    Disease Research Laboratory, Department of Microbiology and Immunology,
    University of Otago, P.O. Box 56, Dunedin, New Zealand.
    Vaccine, (2005 Oct 10) Vol. 23, No. 42, pp. 4999-5008.
    Journal code: 8406899, ISSN: 0264-410X.
    Netherlands
    (CLINICAL TRIAL)
    Journal; Article; (JOURNAL ARTICLE)
    (RESEARCH SUPPORT, NON-U.S. GOV'T)
    English
   Priority Journals
    200511
    Entered STN: 14 Sep 2005
    Last Updated on STN: 11 Nov 2005
    Entered Medline: 10 Nov 2005
    Johne's disease in ruminants is caused by the pathogenic bacterium
    Mycobacterium avium subspecies ***paratuberculosis***
    Currently available Map commercial vaccines protect against clinical
    disease but not infection. In this study, the proprietary Johne's vaccine
    Neoparasec and an aqueous formulation of Map 316F (AquaVax) were tested in
    sheep. Detailed immunological examination of blood and gut-associated
    lymphoid tissues was carried out on animals after vaccination and
    challenge with virulent Map to identify markers of protective immunity.
    Neoparasec vaccination provided significant protection against disease
    while AquaVax did not. Immune animals had stronger cell-mediated
    responses and altered proportions of CD4+, CD8+, CD25+ and B cells in
    blood, spleen and the gut lymphatics, than diseased animals.
                                      ***paratuberculosis*** : immune
    Vaccination of sheep against M.
    parameters and protective efficacy.
    Johne's disease in ruminants is caused by the pathogenic bacterium
    Mycobacterium avium subspecies
                                    ***paratuberculosis*** (Map).
    Currently available Map commercial vaccines protect against clinical
    disease but not infection. In this study, the proprietary Johne's
    vaccine. . .
Vaccines: AD, administration & dosage
    *Bacterial Vaccines: IM, immunology
     CD4-Positive T-Lymphocytes: IM, immunology
     CD8-Positive T-Lymphocytes: IM, immunology
     Disease Models, Animal
        *** Enzyme-Linked Immunosorbent Assay***
        *** Interferon Type II: AN, analysis***
     Intestinal Mucosa: IM, immunology
     Lymphocyte Activation
     Lymphocyte Subsets: IM, immunology
        ****Mycobacterium avium subsp. paratuberculosis: IM, immunology***
```

AN

DN

TT

AII

CS

SO

DT

LA

FS

EM

AB

TΙ

```
****Paratuberculosis: PC, prevention & control***

*** Receptors, Interleukin-2: AN, analysis***
heep
```

\*Sheep Diseases: PC, prevention & control Spleen: IM, immunology

RN \*\*\*82115-62-6 (Interferon Type II) \*\*\*

- L10 ANSWER 7 OF 19 CABA COPYRIGHT 2008 CABI on STN DUPLICATE 2
  - N 2006:49179 CABA <<LOGINID::20080325>>
- DN 20063031176
- TI Inflammatory cytokine gene expression in different types of granulomatous lesions during asymptomatic stages of bovine \*\*\*paratuberculosis\*\*\*
- AU Tanaka, S.; Sato, M.; Onitsuka, T.; Kamata, H.; Yokomizo, Y.
- CS Comparative Pathology Section, Kyushu Research Station, National Institute of Animal Health, Chuzan-cho 2702, Kagoshima 891-0105, Japan. tanakas@affrc.go.jp
- SO Veterinary Pathology, (2005) Vol. 42, No. 5, pp. 579-588. 41 ref. Publisher: American College of Veterinary Pathologists Inc. Lawrence ISSN: 0300-9858 DOI: 10.1354/vp.42-5-579
- CY United States
- DT Journal LA English
- ED Entered STN: 2 Mar 2006
  - Last Updated on STN: 2 Mar 2006
- The granulomatous lesions in bovine \*\*\*paratuberculosis\*\*\* AB have been classified into two types, i.e., the lepromatous type and the tuberculoid type. To clarify the immunopathologic mechanisms at the site of infection, we compared inflammatory cytokine gene expression between the two types of lesions. Samples were obtained from noninfected control cows (n=5) and naturally infected cows (n=7) that were \*\*\*diagnosed\*\*\* by enzyme-linked immunosorbent \*\*\*assay\*\*\* (ELISA) and faecal culture test. Although none of the infected cows showed clinical signs, tuberculoid lesions were observed in five cows (tuberculoid group) and lepromatous lesions in two cows (lepromatous group). Among the cytokines examined by reverse transcription-polymerase chain reaction (RT-PCR), Th2-type cytokines \*\*\*interleukin\*\*\* -4 (IL-4) and IL-10, and Th1-type cytokine IL-2 were expressed more significantly in the lepromatous group than in the tuberculoid (P<0.01) and noninfected groups (P<0.05). No statistical differences were observed in the expression of
  - \*\*\*interferon\*\*\* -gamma, IL-1 beta, TNF-alpha, and GM-CSF among lepromatous, tuberculoid, and noninfected groups. Expression of proinflammatory cytokine IL-12 mRNA, however, did not differ among the three group; IL-18 was expressed at lower levels in the lepromatous group than in the tuberculoid group and the noninfected group (P<0.0001). Moreover, the number of cells in which IL-18 mRNAs were detected by in situ hybridization was markedly decreased in the lepromatous group. These results indicate that the formation of lepromatous-type lesions or tuberculoid-type lesions may be influenced by alterations in Th1/Th2-type cytokine production and that IL-18 may play an important role in a Th1-to-Th2 switch in \*\*\*paratuberculosis\*\*\*
- TI Inflammatory cytokine gene expression in different types of granulomatous lesions during asymptomatic stages of bovine \*\*\*paratuberculosis\*\*\*.

  AB The granulomatous lesions in bovine \*\*\*paratuberculosis\*\*\* have been classified into two types, i.e., the lepromatous type and the tuberculoid

type. To clarify the immunopathologic mechanisms at. . . the two types of lesions. Samples were obtained from noninfected control cows (n=5) and naturally infected cows (n=7) that were \*\*\*diagnosed\*\*\* by \*\*\*assay\*\*\* (ELISA) and faecal culture enzyme-linked immunosorbent test. Although none of the infected cows showed clinical signs, tuberculoid lesions were observed in five. . . and lepromatous lesions in two cows (lepromatous group). Among the cytokines examined by reverse transcription-polymerase chain reaction (RT-PCR), Th2-type cytokines \*\*\*interleukin\*\*\* -4 (IL-4) and IL-10, and Th1-type cytokine IL-2 were

expressed more significantly in the lepromatous group than in the tuberculoid (P<0.01) and noninfected groups (P<0.05). No statistical differences were observed in the expression of \*\*\*interferon\*\*\* -gamma, IL-1 beta, TNF-alpha, and GM-CSF among lepromatous, tuberculoid, and noninfected groups. Expression of proinflammatory cytokine IL-12 mRNA, however, did not. . . influenced by alterations in Th1/Th2-type cytokine production and that IL-18 may play an important role in a Th1-to-Th2 switch in \*\*\*paratuberculosis\*\*\*

- cows; cytokines; disease course; gene expression; genes; granuloma; histopathology; immunopathology; \*\*\*interferon\*\*\*; \*\*\*interleukin\*\*\* \*\*\*interleukin\*\*\* 10; \*\*\*interleukin\*\*\* 2; \*\*\*interleukin\*\*\* \*\*\*interleukins\*\*\*; messenger RNA; \*\*\*paratuberculosis\*\*\*; 4; tumour necrosis factor
- ST \*\*\*interleukin\*\*\* 18

ORGN cattle; Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\*

- L10 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
- AN 2004:1056118 CAPLUS <<LOGINID::20080325>> DN 142:73022
- TΙ
- Analysis of the immune response to Mycobacterium avium subsp. \*\*\*Paratuberculosis\*\*\* in experimentally infected calves
- Koo, Hye Cheong; Park, Yong Ho; Hamilton, Mary Jo; Barrington, George M.; Davies, Christopher J.; Kim, Jong Bae; Dahl, John L.; Waters, W. Ray; Davis, William C.
- Department of Veterinary Microbiology, College of Veterinary Medicine and School of Agricultural Biotechnology, Seoul National University, Seoul, S. Korea
- Infection and Immunity (2004), 72(12), 6870-6883 SO CODEN: INFIBR: ISSN: 0019-9567
- PB American Society for Microbiology
- Journal
- DT
- LA English
- AB Johne's disease of cattle is widespread and causes significant economic loss to producers. Control has been hindered by limited understanding of the immune response to the causative agent, Mycobacterium avium subsp.

\*\*\*paratuberculosis\*\*\* , and lack of an effective vaccine and sensitive specific \*\*\*diagnostic\*\*\* \*\*\*assays\*\*\* . The present study was conducted to gain insight into factors affecting the immune response to M. avium subsp. \*\*\*paratuberculosis\*\*\* . A persistent proliferative response to M. avium subsp. \*\*\*paratuberculosis\*\*\* purified protein deriv. and sol. M. avium subsp. \*\*\*paratuberculosis\*\*\* antigens was detected in orally infected neonatal calves 6 mo postinfection (p.i.) by flow cytometry (FC). CD4+ T cells with a memory phenotype (CD45R0+) expressing CD25 and CD26 were the predominant cell type responding to antigens. Few CD8+ T cells proliferated in response to antigens until 18 mo p.i. .gamma..delta. T cells did not appear to respond to antigen until 18 mo p.i. The majority of WC1+ CD2- and a few WC1- CD2+ .gamma..delta. T cells expressed CD25 at time zero. By 18 mo, however, subsets of

.gamma..delta. T cells from both control and infected animals showed an increase in expression of CD25, ACT2, and CD26 in the presence of the antigens. Two populations of CD3-, non-T non-B null cells, CD2+ and CD2-, proliferated in cell cultures from some control and infected animals during the study, with and without antigen. The studies clearly show multicolor FC offers a consistent reliable way to monitor the evolution and changes in the immune response to M. avium subsp. \*\*\*paratuberculosis\*\*\* that occur during disease progression.

THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE.CNT 65 ALL CITATIONS AVAILABLE IN THE RE FORMAT

- Analysis of the immune response to Mycobacterium avium subsp. \*\*\*Paratuberculosis\*\*\* in experimentally infected calves
- AB . . . to producers. Control has been hindered by limited understanding of the immune response to the causative agent, Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* , and lack of an effective vaccine and sensitive \*\*\*assays\*\*\* . The present study was \*\*\*diagnostic\*\*\* specific conducted to gain insight into factors affecting the immune response to M. avium subsp. \*\*\*paratuberculosis\*\*\* . A persistent proliferative response to M. avium subsp. \*\*\*paratuberculosis\*\*\* purified protein deriv. and sol. M. avium subsp. \*\*\*paratuberculosis\*\*\* antigens was detected in orally infected meonatal calves 6 mo postinfection (p.i.) by flow cytometry (FC). CD4+ T cells with. . . FC offers a consistent reliable way to monitor the evolution and changes in the immune response to M. avium subsp. \*\*\*paratuberculosis\*\*\* that occur during disease progression.
- Mycobacterium infection cattle \*\*\*interleukin\*\*\* \*\*\*interferon\*\*\* ST TCR flow cytometry
- \*\*\*Interleukin\*\*\* TT 2 receptors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha. chain; flow cytometric anal, of immune response to Mycobacterium avium infection in calves)
- тт \*\*\*Interferons\*\*\*
  - RL: BSU (Biological study, unclassified); BIOL (Biological study) (.gamma.; flow cytometric anal. of immune response to Mycobacterium avium infection in calves)
- L10 ANSWER 9 OF 19 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 4
- AN 2004:178760 BIOSIS <<LOGINID::20080325>>
- DN PREV200400179647
- TT Cytokine gene expression in peripheral blood mononuclear cells and tissues of cattle infected with Mycobacterium avium subsp.
  - \*\*\*paratuberculosis\*\*\* : Evidence for an inherent proinflammatory gene expression pattern.
- Coussens, Paul M. [Reprint Author]; Verman, Nitin; Coussens, Marc A.; Elftman, Michael D.; McNulty, Amanda M.
- Department of Animal Science, Michigan State University, 1205H Anthony Hall, East Lansing, MI, 48824, USA coussens@msu.edu
- SO Infection and Immunity, (March 2004) Vol. 72, No. 3, pp. 1409-1422. print. ISSN: 0019-9567 (ISSN print).
- DT Article
- LA English
- ED Entered STN: 31 Mar 2004
  - Last Updated on STN: 31 Mar 2004
- AB In cattle and other ruminants, infection with the intracellular pathogen Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* results in a

granulomatous enteritis (Johne's disease) that is often fatal. The key features of host immunity to M. avium subsp. \*\*\*paratuberculosis\*\*\* infection include an appropriate early proinflammatory and cytotoxic response (Th1-like) that eventually gives way to a predominant antibody-based response (Th2-like). Clinical disease symptoms often appear subsequent to waning of the Th1-like immune response.
Understanding why this shift in the immune response occurs and the underlying molecular mechanisms involved is critical to future control measures and \*\*\*diagnosis\*\*\* . Previous studies have suggested that M. avium subsp. \*\*\*paratuberculosis\*\*\* may suppress gene expression in peripheral blood mononuclear cells (PBMCs) from infected cows, despite a continued inflammatory reaction at sites of infection. In the present study, we tested the hypothesis that exposure to M. avium subsp.

\*\*\*paratuberculosis\*\*\* suppresses a proinflammatory gene expression pattern in PBMCs from infected cows. To do this, we examined expression of genes encoding \*\*\*interleukin\*\*\* -lalpha (IL-lalpha), IL-2, IL-4, IL-5, IL-6, IL-10, IL-12p35, IL-16, and IL-18, as well as genes encoding gamma \*\*\*interferor\*\* (IFN-gamma), transforming growth factor beta (TGF-beta), and tumor necrosis factor alpha (TNF-alpha), in PBMCs, intestinal lesions, and mesenteric lymph nodes of cattle naturally infected with M. avium subsp. \*\*\*paratuberculosis\*\*\*. Cytokine gene expression in these cells and tissues was compared to expression in similar cells and tissues was compared to expression in similar cells and tissues was compared to expression in the comprehensive results demonstrate that for most cytokine genes, including the genes encoding IFN-gamma, TGF-beta, TNF-alpha, IL-1alpha, IL-4, IL-6, IL-8, and IL-12p35, differential expression in FBMCs from infected and control cattle did not require stimulation with M. avium subsp.

\*\*\*paratuberculosis\*\*\* In fact, stimulation with M. avium subop.

\*\*\*paratuberculosis\*\*\* tended to reduce the differential expression
observed in infected and uninfected cows for genes encoding IFN-gamma,
IL-lalpha, and IL-6. Only IL-10 gene expression was consistently enhanced
by M. avium subsp. \*\*\*paratuberculosis\*\*\* stimulation of PBMCs from
subclinically infected cattle. In ileal tissues from M. avium subsp.

\*\*\*paratuberculosis\*\*\* -infected cattle, expression of the genes

## encoding

IFN-gamma, TGF-beta, IL-5, and IL-8 was greater than the expression in comparable tissues from control uninfected cattle, while expression of the gene encoding IL-16 was lower in tissues from infected cattle than in control tissues. Mesenteric lymph nodes draining sites of M. avium subso.

\*\*\*paratuberculosis\*\*\* infection expressed higher levels of IL-lalpha, IL-8, IL-2, and IL-10 mRNA than similar tissues from control uninfected cattle expressed. In contrast, the genes encoding TGF-beta and IL-16 were expressed at lower levels in lymph nodes from infected cattle than in tissues from uninfected cattle. Taken together, our results suggest that cells or other mechanisms capable of limiting proinflammatory responses to M. avium subsp. \*\*\*paratuberculosis\*\*\* develop in infected cattle and that a likely place for development and expansion of these cell populations is the mesenteric lymph nodes draining sites of infection.

- TI Cytokine gene expression in peripheral blood mononuclear cells and tissues of cattle infected with Mycobacterium avium subsp.
  - \*\*\*paratuberculosis\*\*\* : Evidence for an inherent proinflammatory gene expression pattern.
- AB In cattle and other ruminants, infection with the intracellular pathogen Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* results in a granulomatous enteritis (Johne's disease) that is often fatal. The key features of host immunity to M. avium subsp. \*\*\*paratuberculosis\*\*\* infection include an appropriate early proinflammatory and cytotoxic

```
response (Th1-like) that eventually gives way to a predominant
     antibody-based response (Th2-like).. . this shift in the immune
     response occurs and the underlying molecular mechanisms involved is
     critical to future control measures and ***diagnosis*** . Previous
     studies have suggested that M. avium subsp. ***paratuberculosis*** may
     suppress gene expression in peripheral blood mononuclear cells (PBMCs)
     from infected cows, despite a continued inflammatory reaction at sites of
     infection. In the present study, we tested the hypothesis that exposure
     to M. avium subsp. ***paratuberculosis*** suppresses a proinflammatory
     gene expression pattern in PBMCs from infected cows. To do this, we
     examined expression of genes encoding ***interleukin*** -lalpha
     (IL-lalpha), IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p35, IL-16, and
     IL-18, as well as genes encoding gamma ***interferon*** (IFN-gamma),
     transforming growth factor beta (TGF-beta), and tumor necrosis factor
     alpha (TNF-alpha), in PBMCs, intestinal lesions, and mesenteric lymph
     nodes of cattle naturally infected with M. avium subsp.
       ***paratuberculosis*** . Cytokine gene expression in these cells and
     tissues was compared to expression in similar cells and tissues from
     control uninfected. . . IL-8, and IL-12p35, differential expression in
     PBMCs from infected and control cattle did not require stimulation with M.
     avium subsp. ***paratuberculosis*** In fact, stimulation with M. avium subsp. ***paratuberculosis*** tended to reduce the differential
     expression observed in infected and uninfected cows for genes encoding
     IFN-gamma, IL-lalpha, and IL-6. Only IL-10 gene expression was
     consistently enhanced by M. avium subsp. ***paratuberculosis***
     stimulation of PBMCs from subclinically infected cattle. In ileal tissues
     from M. avium subsp.
                           ***paratuberculosis*** -infected cattle,
     expression of the genes encoding IFN-gamma, TGF-beta, IL-5, and IL-8 was
     greater than the expression in comparable tissues from. . . was lower
     in tissues from infected cattle than in control tissues. Mesenteric lymph
     nodes draining sites of M. avium subsp. ***paratuberculosis***
     infection expressed higher levels of IL-lalpha, IL-8, IL-2, and IL-10 mRNA
     than similar tissues from control uninfected cattle expressed. In. . .
     cattle. Taken together, our results suggest that cells or other
     mechanisms capable of limiting proinflammatory responses to M. avium
     subsp. ***paratuberculosis*** develop in infected cattle and that a
     likely place for development and expansion of these cell populations is
     the mesenteric.
        lymph node: blood and lymphatics, digestive system, immune system;
       peripheral blood mononuclear cell: blood and lymphatics, immune system
           ***paratuberculosis*** : bacterial disease, infectious disease,
        genetics, immunology, Johne's disease
            ***Paratuberculosis***
     Chemicals & Biochemicals
       proinflammatory genes: expression pattern
ORGN .
       Vertebrates
ORGN Classifier
       Mycobacteriaceae 08881
     Super Taxa
       Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
        Bacteria: Microorganisms
     Organism Name
       Mycobacterium avium ssp. ***paratuberculosis*** (subspecies):
        pathogen
```

IT

ΤТ

```
Taxa Notes
        Bacteria, Eubacteria, Microorganisms
GEN cattle IFN-gamma gene [cattle ***interferon*** -gamma gene] (Bovidae); cattle IL-1-alpha gene [cattle ***interleukin*** -1-alpha gene]
     (Bovidae); cattle IL-10 gene [cattle ***interleukin*** -10 gene]
     (Bovidae); cattle IL-12p35 gene [cattle ***interleukin*** -12p35 gene]
     (Bovidae); cattle IL-16 gene [cattle ***interleukin*** -16 gene]
     (Bovidae); cattle IL-18 gene [cattle ***interleukin*** -18 gene]
     (Bovidae); cattle IL-2 gene [cattle ***interleukin*** -2 gene]
     (Bovidae); cattle II-2 gene [cattle "Interleukin" - 4 gene] (Bovidae); cattle II-5 gene [cattle "interleukin" - 5 gene] (Bovidae); cattle II-6 gene [cattle "interleukin" - 6 gene]
     (Bovidae); cattle IL-8 gene [cattle ***interleukin*** -8 gene]
     (Bovidae); cattle TGF-beta gene [cattle transforming growth factor-beta
     gene| (Bovidae); cattle TNF-alpha gene (cattle tumor necrosis factor-alpha
     gene] (Bovidae)
L10 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:885718 CAPLUS <<LOGINID::20080325>>
DN 141:363746
     Development of early-stage ***diagnostic*** method for Johne disease
TI
     by using anti-IL-10 antibody
AU
     Momotani, Eiichi; Mori, Yasuvuki
CS
     Natl. Agric. Bio-oriented Res. Org., Natl. Inst. Animal Health, Tsukuba,
     305-0856, Japan
   BRAIN Techno News (2004), 105, 18-24
SO
     CODEN: BTEEEC: ISSN: 1345-5958
PB Noqyo, Seibutsukei Tokutei Sangyo Gijutsu Kenkyu Kiko, Seibutsukei Tokutei
     Sangyo Gijutsu Kenkyu Shien Senta
DT
    Journal; General Review
LA
    Japanese
AB
    A review on early-stage ***diagnosis*** of Johne's disease (
       ***paratuberculosis*** ) in cattle by modified ***interferon***
     .gamma. ELISA ***assay*** using IL-10 neutralizing antibody, and its
     effectiveness.
     Development of early-stage ***diagnostic*** method for Johne disease
TT
     by using anti-IL-10 antibody
     A review on early-stage ***diagnosis*** of Johne's disease (
AB
       ***paratuberculosis*** ) in cattle by modified ***interferon***
     .qamma. ELISA ***assay*** using IL-10 neutralizing antibody, and its
     effectiveness.
     review cattle Johne disease ***diagnosis*** ELISA
                                                             ***interleukin***
     10 antibody; ***paratuberculosis*** cattle ***diagnosis***
       ***interferon*** gamma ELISA review
     Bos taurus
     Mycobacterium avium ***paratuberculosis***
        (early-stage ***diagnosis*** method for Johne's disease using
        anti-IL-10 antibody)
ΙT
       ***Interleukin*** 10
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (early-stage ***diagnosis*** method for Johne's disease using
        anti-IL-10 antibody)
     Immunoassay
        (enzyme-liked immunosorbent ***assav*** ; early-stage
          ***diagnosis*** method for Johne's disease using anti-IL-10
antibody)
TT
      ***Diagnosis***
```

```
(immunodiagnosis; early-stage ***diagnosis*** method for Johne's
        disease using anti-IL-10 antibody)
IT
     Infection
        ( ***paratuberculosis*** , Johne's disease; early-stage
          ***diagnosis*** method for Johne's disease using anti-IL-10
antibody)
    Antibodies and Immunoglobulins
     RL: ARU (Analytical role, unclassified); BSU (Biological study,
     unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (to IL-10; early-stage
                               ***diagnosis*** method for Johne's disease
       using anti-IL-10 antibody)
       ***Interferons***
    RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic
     use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
        (.gamma.; early-stage ***diagnosis*** method for Johne's disease
        using anti-IL-10 antibody)
L10 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN
     2003:472526 CAPLUS <<LOGINID::20080325>>
     139:30816
DN
TΙ
     Peptide T and analogs thereof for the stimulation of cytotoxic T
     lymphocyte (CTL) responses and increasing secretion of ***interferon***
     .gamma. and ***interleukin*** 2, and therapeutic use
TN
    Ruscetti, Francis W.; Ruff, Michael R.
    The Government of the United States of America, as Represented by the
     Secretary Department of Health and Human Services National Institutes of
     Health, USA
    PCT Int. Appl., 43 pp.
SO
     CODEN: PIXXD2
    Patent
T.A
    English
FAN.CNT 1
                      KIND DATE
                                        APPLICATION NO. DATE
     PATENT NO.
    WO 2003050136
                        A2
                             20030619 WO 2002-US39109
PT
                                                                20021206
     WO 2003050136
                        A3
                              20031204
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    AU 2002357093
                        A1
                             20030623
                                          AU 2002-357093
PRAI US 2001-338971P
                         P
                              20011207
     WO 2002-US39109
                         W
                               20021206
    MARPAT 139:30816
    The invention provides a method of increasing cytotoxic T lymphocyte (CTL)
```

3 The invention provides a method of increasing cytotoxic T lymphocyte (CTL) activity in a subject, comprising administering a CTL activity-stimulating ant. of peptide T or an analog thereof. A method of increasing .gamma. \*\*\*interferon\*\*\* (IFN-gamma.) secretion in a subject comprises administering an IFN-gamma. secretion-increasing amt. of peptide T or an analog thereof. A method of increasing \*\*\*interleukin\*\*\* 2 (IL-2)

```
secretion in a subject comprises administering an IL-2
secretion-increasing amt. of peptide T or an analog thereof. A method of
treating a subject ***diagnosed*** as having a disease assocd. with
reduced CTL activity comprises administering a CTL activity-stimulating
amt. of peptide T or an analog thereof. A method of treating a subject
 ***diagnosed*** as having a disease assocd. with reduced IFN-.gamma.
activity comprises administering an IFN-.gamma. activity-stimulating amt.
of peptide T or an analog thereof. A method of treating a subject
 ***diagnosed*** as having a disease assocd. with reduced IL-2 activity
comprises administering an IL-2 activity-stimulating amt. of peptide T or
an analog thereof.
Peptide T and analogs thereof for the stimulation of cytotoxic T
lymphocyte (CTL) responses and increasing secretion of
.gamma. and ***interleukin*** 2, and therapeutic use
. . . in a subject, comprising administering a CTL activity-stimulating
amt. of peptide T or an analog thereof. A method of increasing .gamma .-
 ***interferon*** (IFN-.gamma.) secretion in a subject comprises
administering an IFN-.gamma. secretion-increasing amt. of peptide T or an
analog thereof. A method of increasing ***interleukin*** 2 (IL-2)
secretion in a subject comprises administering an IL-2
secretion-increasing amt. of peptide T or an analog thereof. A method of
treating a subject ***diagnosed*** as having a disease assocd. with
reduced CTL activity comprises administering a CTL activity-stimulating
amt. of peptide T or an analog thereof. A method of treating a subject
 ***diagnosed*** as having a disease assocd. with reduced IFN-.gamma.
activity comprises administering an IFN-.gamma. activity-stimulating amt.
of peptide T or an analog thereof. A method of treating a subject
 ***diagnosed*** as having a disease assocd. with reduced IL-2 activity
comprises administering an IL-2 activity-stimulating amt. of peptide T or
an. . .
peptide T analog cytotoxic T lymphocyte response stimulation;
 ***interferon*** gamma secretion peptide T; ***interleukin*** 2
secretion peptide T
Lymphoma
   (B-cell; peptide T and analogs for stimulation of cytotoxic T
  lymphocyte responses and increasing secretion of ***interferon***
  .gamma. and ***interleukin*** 2, and therapeutic use)
Lymphoma
  (T-cell; peptide T and analogs for stimulation of cytotoxic T
  lymphocyte responses and increasing secretion of ***interferon***
```

\*\*\*interleukin\*\*\* 2, and therapeutic use) ΙT Tumor necrosis factors RL: BSU (Biological study, unclassified); BIOL (Biological study) (TNF-.alpha.; peptide T and analogs for stimulation of cytotoxic T lymphocyte responses and increasing secretion of \*\*\*interferon\*\*\* .gamma. and \*\*\*interleukin\*\*\* 2, and therapeutic use)

ΙT Carcinoma

TI

ΔB

ΙT

ΙT

(adenocarcinoma; peptide T and analogs for stimulation of cytotoxic T lymphocyte responses and increasing secretion of \*\*\*interferon\*\*\* .gamma. and \*\*\*interleukin\*\*\* 2, and therapeutic use)

AIDS (disease)

.gamma. and

(and AIDS-related lymphoma or sarcoma; peptide T and analogs for stimulation of cytotoxic T lymphocyte responses and increasing secretion of \*\*\*interferon\*\*\* .gamma. and \*\*\*interleukin\*\*\* 2, and therapeutic use)

ΙT Infection

(bacterial; peptide T and analogs for stimulation of cytotoxic T

```
lymphocyte responses and increasing secretion of ***interferon***
        .gamma. and ***interleukin*** 2, and therapeutic use)
    Esophagus, neoplasm
    Head and Neck, neoplasm
    Head and Neck, neoplasm
        (carcinoma; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Uterus, neoplasm
       (cervix, carcinoma; peptide T and analogs for stimulation of cytotoxic
       I lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Carcinoma
ΙT
    Uterus, neoplasm
        (cervix; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Intestine, neoplasm
       (colon; peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
ΤТ
    Intestine, neoplasm
        (colorectal; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    T cell (lymphocyte)
ΙT
        (cytotoxic; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Carcinoma
        (esophageal; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ΙT
    Mycosis
        (fungoides; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Neuroglia, neoplasm
       (glioblastoma; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ТТ
    Carcinoma
    Carcinoma
        (head and neck squamous cell carcinoma; peptide T and analogs for
       stimulation of cytotoxic T lymphocyte responses and increasing
       secretion of ***interferon*** .gamma. and ***interleukin*** 2,
       and therapeutic use)
TT
   Carcinoma
    Carcinoma
```

lymphocyte responses and increasing secretion of \*\*\*interferon\*\*\*
.gamma. and \*\*\*interleukin\*\*\* 2, and therapeutic use)

(blastoma; peptide T and analogs for stimulation of cytotoxic T lymphocyte responses and increasing secretion of \*\*\*interferon\*\*\*.camma.and \*\*\*interleukin\*\*\* 2, and therapeutic use)

(cancer; peptide T and analogs for stimulation of cytotoxic T

IT

ΙT

Neoplasm

Urogenital system

```
(head and neck; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma, and ***interleukin*** 2, and therapeutic use)
ΙT
   Neoplasm
       (histiocytoma; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
TТ
   Hypoxia
        (hypoxic tumors; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
TТ
    Fungi
    Parasite
       (infection; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ΤТ
   Carcinoma
       (laryngeal squamous cell; peptide T and analogs for stimulation of
       cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
ΙT
    Neoplasm
        (metastasis; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Skin, neoplasm
       (mycosis fungoides; peptide T and analogs for stimulation of cytotoxic
       T lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Histiocyte
       (neoplasm, histiocytoma; peptide T and analogs for stimulation of
       cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
    Nerve, neoplasm
        (neuroblastoma; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
TT
    Lymphoma
       (non-Hodgkin's; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Carcinoma
       (oral squamous cell; peptide T and analogs for stimulation of cytotoxic
       T lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ΤТ
    Actinobacillus pleuropneumoniae
    Adenoma
    Alternaria alternata
    Anti-AIDS agents
    Antibacterial agents
    Antimalarials
    Antitumor agents
    Antiviral agents
    Aspergillus fumigatus
```

Bacillus anthracis Bladder, neoplasm

Blastomyces dermatitidis

Brain, neoplasm Brucella

Brucella melitensis

CD8-positive T cell

Campylobacter

Candida albicans Carcinoma

Carcinoma

Chlamydia pneumoniae

Chlamydia trachomatis Chlamydophila psittaci

Clostridium

Clostridium tetani

Coccidioides immitis

Coronavirus Coxiella burnetii

Cryptococcus neoformans

Dengue virus

Eastern equine encephalitis virus

Eastern equ. Ebola virus

Ehrlichia

Ehrlichia ruminantium

Entamoeba histolytica

Escherichia coli

Fungicides

Haemophilus

Haemophilus ducrevi

Haemophilus influenzae

Hantavirus

Hematopoietic neoplasm

Hepatitis A virus

Hepatitis B virus

Hepatitis C virus

Hepatitis E virus

Hepatitis delta virus Histoplasma capsulatum

Hodgkin's disease

Human

Human T-lymphotropic virus 1

Human adenovirus

Human coxsackievirus

Human immunodeficiency virus

Human immunodeficiency virus 1

Human immunodeficiency virus 2

Human papillomavirus

Human poliovirus Immunostimulants

Influenza A virus

Influenza B virus

Japanese encephalitis virus

Kidney, neoplasm

Lassa virus

Legionella

Legionella pneumophila

```
Leishmania
Leishmania major
Leukemia
Listeria ivanovii
Listeria monocytogenes
Liver, neoplasm
Lung, neoplasm
Lymphoma
Mammary gland, neoplasm
Mannheimia haemolytica
Marburg virus
Measles virus
Melanoma
Multiple myeloma
Mumps virus
Murray Valley encephalitis virus
Mycobacterium BCG
Mycobacterium africanum
Mycobacterium avium
                      ***paratuberculosis***
Mycobacterium avium
Mycobacterium bovis
Mycobacterium intracellulare
Mycobacterium kansasii
Mycobacterium marinum
Mycobacterium tuberculosis
Mycobacterium ulcerans
Myeloid leukemia
Neisseria gonorrhoeae
Neisseria meningitidis
Neoplasm
Nervous system, neoplasm
Neuroglia, neoplasm
Nocardia
Nocardia asteroides
Ovary, neoplasm
Pancreas, neoplasm
Paracoccidioides brasiliensis
Parasiticides
Pasteurella
Pasteurella multocida
Penicillium marneffei
Plasmodium (malarial genus)
Plasmodium falciparum
Plasmodium malariae
Plasmodium vivax
Pneumocystis carinii
Polyomavirus
Prostate gland, neoplasm
Pseudomonas
Pseudomonas aeruginosa
Rabies virus
Respiratory syncytial virus
Rhinovirus
Rickettsia
Rift Valley fever virus
```

Rotavirus A Rotavirus B

```
Rotavirus C
    Rous sarcoma virus
    Rubella virus
    Salmonella
    Salmonella typhi
    Sarcoma
    Schistosoma
    Schistosoma mansoni
    Shigella
    Simian immunodeficiency virus
    Sindbis virus
    Skin, neoplasm
    St. Louis encephalitis virus
    Staphylococcus aureus
    Staphylococcus epidermidis
    Streptococcus agalactiae
    Streptococcus pyogenes
    Testis, neoplasm
    Toxoplasma gondii
    Trypanosoma brucei
    Trypanosoma cruzi
    Variola virus
    Vesicular stomatitis virus
    Vibrio cholerae
    West Nile virus
    Yellow fever virus
    Yersinia
    Yersinia enterocolitica
    Yersinia pestis
        (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
    Cytokines
        ***Interleukin***
        ***Interleukin*** 10
        ***Interleukin*** 12
        ***Interleukin*** 13
        ***Interleukin***
        ***Interleukin***
                           4
        ***Interleukin***
                            6
        ***Interleukin***
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
    Peptides, biological studies
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
    (Biological study); USES (Uses)
        (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
   Carcinoma
       (pulmonary squamous cell; peptide T and analogs for stimulation of
       cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
```

use)

ΙT

TТ

```
TT
   Neoplasm
        (solid, carcinoma; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Head and Neck, neoplasm
    Head and Neck, neoplasm
    Larvnx, neoplasm
    Lung, neoplasm
    Mouth, neoplasm
        (squamous cell carcinoma; peptide T and analogs for stimulation of
       cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
ΤТ
    Carcinoma
       (squamous cell; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and
                     ***interleukin*** 2, and therapeutic use)
ΙT
   Pharvnx, neoplasm
       (throat squamous cell carcinoma; peptide T and analogs for stimulation
       of cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
    Infection
       (viral; peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .qamma. and
         ***interleukin*** 2, and therapeutic use)
       ***Interferons***
ΙT
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (.gamma.; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
        .gamma. and ***interleukin*** 2, and therapeutic use)
    106362-32-7D, C-terminal derivs.
    RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
    use); BIOL (Biological study); USES (Uses)
        (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
    106362-32-7, Peptide T 106362-32-7D, Peptide T, analogs
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
    (Biological study); USES (Uses)
        (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
    107531-09-9 107531-11-3 107531-12-4 107531-14-6 118936-25-7
    118936-26-8 118936-27-9 118936-30-4 118936-31-5 118936-32-6
    118957-86-1 119386-95-7
    RL: PRP (Properties)
       (unclaimed sequence; peptide T and analogs thereof for the stimulation
       of cytotoxic T lymphocyte (CTL) responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
L10 ANSWER 12 OF 19 MEDLINE on STN
AN 2002454621 MEDLINE <<LOGINID::20080325>>
```

- DN PubMed ID: 12208110
- TI Localisation of CD25+ cells and MHCII+ cells in lymph nodes draining Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* vaccination granuloma and the presence of a systemic immune response.
- AU Valheim M; Hasvold H J; Storset A K; Larsen H J S; Press C McL
- CS Department of Morphology, Genetics and Aquatic Biology, Norwegian School of Veterinary Science, P.O. Box 8146 Dep. N-0033 Oslo, Norway.. mette.valheim@vetinst.no
- SO Research in veterinary science, (2002 Aug) Vol. 73, No. 1, pp. 77-85. Journal code: 0401300. ISSN: 0034-5288.
- CY England: United Kingdom
- DT (CLINICAL TRIAL)
  Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 200305
- ED Entered STN: 6 Sep 2002
  - Last Updated on STN: 21 May 2003 Entered Medline: 20 May 2003
- AB Vaccination of goat kids against \*\*\*paratuberculosis\*\*\* protects against lesions and clinical disease. The systemic cellular response was studied in goat kids 3-9 weeks after vaccination. Peripheral blood cells showed increased \*\*\*interferon\*\*\* -gamma production and expression of \*\*\*interleukin\*\*\* -2 receptor (CD25) after stimulation with

## Mycobacterium

avium subsp. \*\*\*paratuberculosis\*\*\* antigens. The lymph node draining the vaccination granuloma was studied three weeks after vaccination in a parallel group of goat kids. In deep cortex, MHCII+ cells were observed surrounded by CD4+ T-cells, while follicular hypertrophy and hyperplasia were prominent in the subcapsular region and along connective tissue trabecula. Comparison of the local and systemic immune responses revealed an inverse relationship between CD2+ T-cells in the lymph node deep cortex and cells in peripheral blood that up-regulate CD25 upon in vitro stimulation, suggesting that activated and regulatory T-cells in the local lymph node influence the level of circulating antigen-specific T-cells following vaccination against \*\*\*paratuberculosis\*\*\* in goats.

- TI Localisation of CD25+ cells and MHCII+ cells in lymph nodes draining Mycobacterium avium subsp. \*\*\*paratuberculosi\*\*\* vaccination granuloma and the presence of a systemic immune response.
- AB Vaccination of goat kids against \*\*\*paratuberculosis\*\*\* protects against lesions and clinical disease. The systemic cellular response was studied in goat kids 3-9 weeks after vaccination. Peripheral blood cells showed increased \*\*\*interferon\*\*\* -gamma production and expression of \*\*\*interleukin\*\*\* -2 receptor (CD2) after stimulation with

#### Mycobacterium

avium subsp. \*\*\*paratuberculosis\*\*\* antigens. The lymph node draining the vaccination granuloma was studied three weeks after vaccination in a parallel group of goat. . . that activated and regulatory T-cells in the local lymph node influence the level of circulating antigen-specific T-cells following vaccination against \*\*\*paratuberculosis\*\*\* in goats.

CT Check Tags: Male

Animals

Antigens, Bacterial: IM, immunology \*Bacterial Vaccines: IM, immunology

\*\*\* Enzyme-Linked Immunosorbent Assay\*\*\*
Gene Expression Regulation

Goat Diseases: IM, immunology

```
Goat Diseases: MI, microbiology
     Goat Diseases: PA, pathology
     Goat Diseases: . . IM, immunology
     Goats: MI, microbiology
     *Granuloma: IM, immunology
     Granuloma: MI, microbiology
     Granuloma: PA, pathology
     *Histocompatibility Antigens Class II: IM, immunology
         *** Interferon Type II: IM, immunology***
         *** Interferon Type II: ME, metabolism***
      Lymph Nodes: CY, cytology
     *Lymph Nodes: IM, immunology
      Lymph Nodes: MI, microbiology
         ****Mycobacterium avium subsp. paratuberculosis: IM, immunology***
         *** Mycobacterium avium subsp. paratuberculosis: IP, isolation &***
         purification ***
         *** Paratuberculosis: IM, immunology***
         *** Paratuberculosis: MI, microbiology***
         *** Paratuberculosis: PA, pathology***
         *** Paratuberculosis: PC, prevention & control***
         *** Receptors, Interleukin-2: AN, analysis***
         ****Receptors, Interleukin-2: IM, immunology***
     *T-Lymphocytes: IM, immunology
       ***82115-62-6 (Interferon Type II) ***
CM
     0 (Antigens, Bacterial); 0 (Bacterial Vaccines); 0 (Histocompatibility
     Antigens Class II); 0 (Receptors, ***Interleukin*** -2)
L10 ANSWER 13 OF 19
                        MEDI-INE on STN
AN
    2002648148
                  MEDLINE <<LOGINID::20080325>>
DN
     PubMed ID: 12406650
    Type 1 and type 2 responses in regulation of Iq isotype expression in
     cattle.
    Estes D Mark; Brown Wendy C
AU
CS
    Program for the Prevention of Animal Infectious Diseases, Department of
    Veterinary Pathobiology, University of Missouri, Columbia, MO 65211, USA..
     estesd@missouri.edu
    Veterinary immunology and immunopathology, (2002 Nov) Vol. 90, No. 1-2,
SO
    pp. 1-10. Ref: 90
     Journal code: 8002006. ISSN: 0165-2427.
CY
    Netherlands
DT
    Journal; Article; (JOURNAL ARTICLE)
    General Review; (REVIEW)
LA
   English
FS
    Priority Journals
EM
    200305
    Entered STN: 31 Oct 2002
     Last Updated on STN: 3 May 2003
     Entered Medline: 2 May 2003
   Regulation of humoral immune responses is multifactorial involving
     factors. Polarized type 1 or type 2 humoral responses in the laboratory
```

RN

appropriate activation, costimulation and the presence of specific soluble mouse have been linked to expression of specific cytokines and thus can be used to provide insight into the type of response generated by infection. For example, IFN-gamma has been linked to IgG2a and IgG3 production, IL-4 to IgG1 and IgE production and TGF-beta to IgA production. Unlike the laboratory mouse, generally housed under defined conditions, highly skewed isotype expression patterns generally occur in cattle in chronic

infections. A few examples of polarized responses have been noted in chronic experimental or naturally occurring infections including F. hepatica, M. \*\*\*paratuberculosis\*\*\* , C. parvum and B. abortus. In vitro studies using purified bovine B cells and various forms of costimulation and cytokines have demonstrated that isotype responses can be polarized under certain experimental conditions in vitro. That is, IqG1 expression is positively regulated by IL-4 and IqG2 expression is positively regulated by IFN-gamma. Other as yet unidentified factors may play pivotal roles in regulating humoral immune responses in large ruminant species in vivo. This possibility is best exemplified by recent studies using DNA vaccines in cattle that have been demonstrated in the mouse to be generally polarizing to a type 1 response. Surprisingly, studies in cattle using plasmid DNA as vaccination material show an almost exclusive IgG1 response. Based on a number of studies using T cell clones and various biological \*\*\*assays\*\*\* , it is clear that the classical roles of many cytokines in the laboratory mouse do not extrapolate entirely or at all to cattle. Thus, the design of adjuvants and immune modulators should be based on studies done in cattle or using bovine cells. Based on studies to date, several "holes" in the cytokine repertoire exist and these roles may be assumed by unique factors or activities of other known cytokines.

AB . . A few examples of polarized responses have been noted in chronic experimental or naturally occurring infections including F. hepatica, M.

\*\*\*paratuberculosis\*\*\* , C. parvum and B. abortus. In vitro studies using purified bovine B cells and various forms of costimulation and cytokines. . . material show an almost exclusive IgGl response. Based on a number of studies using T cell clones and various biological

\*\*\*assays\*\*\* , it is clear that the classical roles of many cytokines in

the laboratory mouse do not extrapolate entirely or at. . . Animals

\*Cattle: IM, immunology

\*Gene Expression Regulation

\*Immunoglobulin Isotypes: GE, genetics

\*\*\* Interferon Type II: IM, immunology\*\*\*

\*\*\* Interleukins: IM, immunology\*\*\*

\*Th1 Cells: IM, immunology

\*Th2 Cells: IM, immunology

Transforming Growth Factor beta: IM, immunology

RN \*\*\*82115-62-6 (Interferon Type II) \*\*\*

- CN 0 (Immunoglobulin Isotypes); 0 ( \*\*\*Interleukins\*\*\* ); 0 (Transforming Growth Factor beta)
- L10 ANSWER 14 OF 19 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
- AN 2001:570180 BIOSIS <<LOGINID::20080325>>
- DN PREV200100570180

CT

- TI Results of multiple \*\*\*diagnostic\*\*\* tests for Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* in patients with inflammatory bowel disease and in controls.
- AU Collins, Michael T. [Reprint author]; Lisby, Gorm; Moser, Claus; Chicks, Debra; Christensen, Steen; Reichelderfer, Mark; Hoiby, Niels; Harms, Bruce A.; Thomsen, Ole O.; Skibsted, Ulrik; Binder, Vibeke
- CS Department of Pathobiological Sciences, School of Veterinary Medicine, 2015 Linden Dr. West, Madison, WI, 53706-1102, USA moollin9ffacstaff, wisc.edu
- SO Journal of Clinical Microbiology, (December, 2001) Vol. 38, No. 12, pp. 4373-4381. print.

vaccinated (CD, 77.5%; UC, 86.6%; controls, 83.0%) whereas none of the U.S. patients with IBD and only 2% of U.S. controls were vaccinated. Among Danish IBD patients, positive PCR findings were four times more common among subjects who were not BCG vaccinated (33.3%) than among BCG vaccinates (8.8%, P=0.02). Culture of the same tissues tested by PCR using modified BACTEC 12B medium failed to grow M. avium subsp. \*\*\*paratuberculosis\*\*\* from patients or controls. U.S. CD patients had the highest serological evidence (enzyme-linked immunosorbent \*\*\*assay\*\*\* (ELISA) for serum antibodies) of M. avium subsp. \*\*\*paratuberculosis\*\*\* infection (20.7% of patients positive) which was higher than for all UC patients studied (6.1%) or healthy controls (3.8%, P<0.005). Among Danish patients alone, however, no significant differences in rates of ELISA-positive results among CD, UC, or control patients were found. For 181 study subjects, both IS900 PCR and ELISA were performed. Although 11 were ELISA positive and 36 were PCR positive, in no instance was a patient positive by both tests, suggesting that these states are mutually exclusive. Evaluation of cytokine-mediated immune responses of IBD patients was complicated by the influence of immunosuppressive therapy given most IBD patients. Gamma \*\*\*interferon\*\*\* (IFN-gamma) release by peripheral blood leukocytes after M. avium purified protein derivative PPD antigen stimulation showed significantly lower responses in CD patients than in UC patients or controls in both U.S. (by ex vivo \*\*\*assay\*\*\* ) and Danish (by in vitro \*\*\*assay\*\*\* ) populations (P<0.05). \*\*\*Interleukin\*\*\* -5 responses were not different among CD, UC, or control groups. Collectively, the PCR, ELISA, and IFN-gamma tests for M. avium subsp. \*\*\*paratuberculosis\*\*\* together with the unexpected observation that BCG vaccination influenced M. avium subsp. \*\*\*paratuberculosis\*\*\* detection, lead us to conclude that M. avium subsp.

\*\*\*paratuberculosis\*\*\* , or some similarly fastidious mycobacterial species, infects at least a subset of IBD patients. Whether the infection

is primary (causal) or secondary, it may contribute to the

etiopathogenesis of IBD.

CODEN: JCMIDW. ISSN: 0095-1137.

AB Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* has been

have been relatively small and generally only used a single

incriminated as a cause of Crohn's disease (CD); however, studies to date

\*\*\*diagnostic\*\*\*

\*\*\*assay\*\*\*
. The objective of the study was to reexamine the association of M. avium subsp. \*\*\*paratuberculosis\*\*\* and CD using multiple \*\*\*diagnostic\*\*\* tests. Five methods were used to detect M. avium subsp. \*\*\*paratuberculosis\*\*\* infections in 439 inflammatory bowel disease (IBD) patients and 324 control subjects in the United States and Denmark. Most \*\*\*assays\*\*\* were adaptations of \*\*\*diagnostic\*\*\* tests for this infection performed routinely on animals. PCR for IS900, a genetic element unique to M. avium subsp. \*\*\*paratuberculosis\*\*\*, was positive significantly more often on resected bowel and lymph node tissues from CD patients (19.0%) and ulcerative colitis (UC) patients (26.2%) than from controls (6.3%) (Fv0.05). Positive IS900 FCR results occurred more often in U.S. than in Danish IBD patients, 32.0 versus 13.3% (P=0.025). The majority of Danish patients were bacillus Calmette-Guerin (Mycobacterium bovis BCG)

Entered STN: 12 Dec 2001 Last Updated on STN: 25 Feb 2002

DT

LA English

Article

```
Results of multiple ***diagnostic*** tests for Mycobacterium avium
    subsp. ***paratuberculosis*** in patients with inflammatory bowel
    disease and in controls.
AB Mycobacterium avium subsp. ***paratuberculosis*** has been
    incriminated as a cause of Crohn's disease (CD); however, studies to date
    have been relatively small and generally only used a single
      reexamine the association of M. avium subsp. ***paratuberculosis***
    and CD using multiple ***diagnostic*** tests. Five methods were used to detect M. avium subsp. ***paratuberculosis*** infections in 439
    inflammatory bowel disease (IBD) patients and 324 control subjects in the
    United States and Denmark. Most ***assays*** were adaptations of
      ***diagnostic*** tests for this infection performed routinely on
    animals. PCR for IS900, a genetic element unique to M. avium subsp.
      ***paratuberculosis*** , was positive significantly more often on
    resected bowel and lymph node tissues from CD patients (19.0%) and
    ulcerative colitis (UC). . . P=0.02). Culture of the same tissues
    tested by PCR using modified BACTEC 12B medium failed to grow M. avium
    subsp. ***paratuberculosis*** from patients or controls. U.S. CD
    patients had the highest serological evidence (enzyme-linked immunosorbent
       ***assav*** (ELISA) for serum antibodies) of M. avium subsp.
      ***paratuberculosis*** infection (20.7% of patients positive) which was
    higher than for all UC patients studied (6.1%) or healthy controls (3.8%,
    P<0.005).. . of cytokine-mediated immune responses of IBD patients
    was complicated by the influence of immunosuppressive therapy given most
    IBD patients. Gamma ***interferon*** (IFN-gamma) release by
    peripheral blood leukocytes after M. avium purified protein derivative PPD
    antigen stimulation showed significantly lower responses in CD patients
    than in UC patients or controls in both U.S. (by ex vivo ***assay*** )
    and Danish (by in vitro ***assay*** ) populations (P<0.05).
      ***Interleukin*** -5 responses were not different among CD, UC, or
    control groups. Collectively, the PCR, ELISA, and IFN-gamma tests for M.
    avium subsp. ***paratuberculosis*** together with the unexpected
    observation that BCG vaccination influenced M. avium subsp.
      ***paratuberculosis*** detection, lead us to conclude that M. avium
    subsp. ***paratuberculosis*** , or some similarly fastidious
    mycobacterial species, infects at least a subset of IBD patients. Whether
    the infection is primary (causal). . .
ΙT
    . . .
       system disease
       Crohn Disease (MeSH)
IT
       inflammatory bowel disease: digestive system disease
       Inflammatory Bowel Diseases (MeSH)
    Chemicals & Biochemicals
       IFN-gamma [ ***interferon*** -gamma]; PPD antigen
ΙT
    Methods & Equipment
       ELISA: analytical method, labeling; PCR [polymerase chain reaction]:
       DNA amplification, ***diagnostic*** method, in situ recombinant
       gene expression detection, sequencing techniques
       Vertebrates
ORGN Classifier
       Mycobacteriaceae 08881
    Super Taxa
       Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
       Bacteria; Microorganisms
```

Organism Name
Mycobacterium avium ssp. \*\*\*paratuberculosis\*\*\* : pathogen
Mycobacterium bovis: pathogen
Taxa Notes

Bacteria, Eubacteria, Microorganisms

- L10 ANSWER 15 OF 19 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 5
- AN 2001:410237 BIOSIS <<LOGINID::20080325>>
- DN PREV200100410237
- TI Subclinical \*\*\*paratuberculosis\*\*\* in goats following experimental infection: An immunological and microbiological study.
- AU Storset, A. K. [Reprint author]; Hasvold, H. J.; Valheim, M.; Brun-Hansen, H.; Berntsen, G.; Whist, S. K.; Djonne, B.; Press, C. McL.; Holstad, G.; Larsen, H. J. S.
- CS Department of Pharmacology, Microbiology and Food Hygiene, Norwegian School of Veterinary Science, N-0033, Oslo, Norway anne.storset@veths.no
- SO Veterinary Immunology and Immunopathology, (10 August, 2001) Vol. 80, No. 3-4, pp. 271-287, print. CODEN: VIIMOS. ISSN: 0165-2427.
- DT Article

9

the

- LA English
- ED Entered STN: 29 Aug 2001
- Last Updated on STN: 22 Feb 2002
- AB An experimental oral infection of goats with a caprine isolate of Mycobacterium a. subsp. \*\*\*paratuberculosis\*\*\* was used to investigate immunological and bacteriological events during the subclinical phase of infection. Seven goats at 5-8 weeks of age were given a bacterial suspension in milk-replacement three times weekly for 9 weeks. Six animals were kept as controls. Cellular recall responses against M. a.

  \*\*\*paratuberculosie\*\*\* were analysed by means of a lymphocyte proliferation test, an ITM-gamma \*\*\*assay\*\*\*\* and an IL-2 receptor
  - proliferation test, an IFN-gamma \*\*\*assay\*\*\* and an IL-2 receptor 
    \*\*\*assay\*\*\* . All inoculated animals had detectable CMI responses from

weeks post-inoculation and through the 2 years of study, although the responses were highest during the first year. Antibodies against M. a. \*\*\*paratuberculosis\*\*\* could be detected from weeks 15-20 in four of

seven animals, and one additional animal became antibody positive at week 35, while two inoculated animals did not produce significant antibody titres during the experiment. At about 1-year post-inoculation, two animals became faecal shedders, while two others started to excrete bacteria into faeces about 2 years post-inoculation. The appearance of M. a. \*\*\*paratuberculosis\*\*\* In faeces was not associated with a decline in cellular responses as far as could be assessed using the current methods for measuring CMI. Pathological lesions due to M. a.

\*\*\*paratuberculosis\*\*\* infection and presence of bacteria were recorded in the intestine and/or mesenteric lymph nodes of five animals while lymph node changes suggestive of \*\*\*paratuberculosis\*\*\* were observed in one animal. Only the two animals with no signs of an active infection at necropsy showed a considerable decline in the cellular parameters during the last year of the study, particularly in the IFN-gamma \*\*\*assay\*\*\*. The two animals with the highest levels of M. a. \*\*\*paratuberculosis\*\*\* responsive CD8+ lymphocytes in the circulation about l-year post-inoculation had no detectable lesions in the distal ileum and colon at necropsy, while high numbers of gammadelta T-cells responsive to M. a.

```
***paratuberculosis*** in the circulation were associated with
    disseminated lesions in the distal ileum and colon.
    Subclinical ***paratuberculosis*** in goats following experimental
     infection: An immunological and microbiological study.
    An experimental oral infection of goats with a caprine isolate of
    Mycobacterium a. subsp. ***paratuberculosis*** was used to investigate
     immunological and bacteriological events during the subclinical phase of
     infection. Seven goats at 5-8 weeks of. . . in milk-replacement three
     times weekly for 9 weeks. Six animals were kept as controls. Cellular
    recall responses against M. a. ***paratuberculosis*** were analysed by means of a lymphocyte proliferation test, an IFN-gamma ***assay*** and
     an IL-2 receptor ***assay*** . All inoculated animals had detectable
     CMI responses from 9 weeks post-inoculation and through the 2 years of
     study, although the responses were highest during the first year.
     Antibodies against M. a. ***paratuberculosis*** could be detected from
     weeks 15-20 in four of the seven animals, and one additional animal became
     antibody positive at. . . faecal shedders, while two others started to
     excrete bacteria into faeces about 2 years post-inoculation. The
     appearance of M. a. ***paratuberculosis*** in faeces was not
     associated with a decline in cellular responses as far as could be
     assessed using the current methods for measuring CMI. Pathological
     lesions due to M. a. ***paratuberculosis*** infection and presence of
     bacteria were recorded in the intestine and/or mesenteric lymph nodes of
     five animals while lymph node changes suggestive of
       ***paratuberculosis*** were observed in one animal. Only the two
     animals with no signs of an active infection at necropsy showed a
     considerable decline in the cellular parameters during the last year of
     the study, particularly in the IFN-gamma ***assay*** . The two animals
     with the highest levels of M. a. ***paratuberculosis*** responsive
     CD8+ lymphocytes in the circulation about 1-year post-inoculation had no
    detectable lesions in the distal ileum and colon at necropsy, while high
     numbers of gammadelta T-cells responsive to M. a. ***paratuberculosis***
     in the circulation were associated with disseminated lesions in the distal
     ileum and colon.
TТ
       digestive system; lymphocyte: blood and lymphatics, immune system;
       mesenteric lymph node: blood and lymphatics, digestive system, immune
       system
TТ
    Diseases
           ***paratuberculosis*** : bacterial disease, subclinical
            ***Paratuberculosis*** (MeSH)
ΙT
     Chemicals & Biochemicals
        IFN-gamma [ ***interferon*** -gammal; IL-2 receptor [
          ***interleukin*** -2 receptor]
    Methods & Equipment
        IFN-qamma ***assay*** : analytical method; ***interleukin*** -2
        receptor ***assay*** : analytical method; lymphocyte proliferation
        test: analytical method; necropsy: analytical method
    Miscellaneous Descriptors
       cellular immunity
       Mammals, Vertebrates
ORGN Classifier
       Mycobacteriaceae 08881
     Super Taxa
       Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
        Bacteria; Microorganisms
```

Organism Name
Mycobacterium avium \*\*\*paratuberculosis\*\*\* : pathogen
Taxa Notes

Bacteria, Eubacteria, Microorganisms

- L10 ANSWER 16 OF 19 LIFESCI COPYRIGHT 2008 CSA on STN DUPLICATE 6
  - N 2001:53334 LIFESCI <<LOGINID::20080325>>
- TI Results of Multiple \*\*\*Diagnostic\*\*\* Tests for Mycobacterium avium subsp. \*\*\*Paratuberculosis\*\*\* in Patients with Inflammatory Bowel Disease and in Controls
- AU Collins\*, M.T.; Lisby, G.; Moser, C.; Chicks, D.; Christensen, S.; Reichelderfer, M.; Hoeiby, N.; Harms, B.A.; Thomsen, O.O.; Skibsted, U.; Binder, V.
- CS Department of Pathobiological Sciences, School of Veterinary Medicine, 2015 Linden Dr. West, Medison, WI 53706-1102; E-mail: mcollin5@facstaff.wisc.edu
- SO Journal of Clinical Microbiology [J. Clin. Microbiol.], (20001200) vol. 38, no. 12, pp. 4373-4381. ISSN: 0095-1137.
- DT Journal
- FS J; A LA English
  - A English
- SL English
- AB Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* has been incriminated as a cause of Crohn's disease (CD); however, studies to date have been relatively small and generally only used a single

  - animals. FCR for IS900, a genetic element unique to M. avium subsp. \*\*\*paratuberculosis\*\* , was positive significantly more often on resected bowel and lymph node tissues from CD patients (19.0%) and ulcerative colitis (UC) patients (26.2%) than from controls (6.3%) (P < 0.05). Positive IS900 PCR results occurred more often in U.S. than in Danish IBD patients, 32.0 versus 13.3% (P = 0.025). The majority of Danish patients were bacillus Calmette-Guerin (Mycobacterium bovis BCG) vaccinated (CD, 77.5%) UC, 86.6%; controls, 83.0%) whereas none of the U.S. patients with IBD and only 2% of U.S. controls were vaccinated. Among Danish IBD patients, positive PCR findings were four times more common manng subjects who were not BCG vaccinated (33.3%) than among BCG vaccinates (8.8%, P = 0.02). Culture of the same tissues tested by PCR using modified BACTEC 128 medium failed to grow M. avium subsp.
  - \*\*\*paratuberculosis\*\*\* from patients or controls. U.S. CD patients had the highest serological evidence (enzyme-linked immunosorbent
    \*\*\*assay\*\*\* [ELISA] for serum antibodies) of M. avium subsp.
  - \*\*\*paratuberculosis\*\*\* infection (20.7% of patients positive) which was higher than for all UC patients studied (6.1%) or healthy controls (3.8%, P < 0.005). Among Danish patients alone, however, no significant differences in rates of ELISA-positive results among CD, UC, or control patients were found. For 181study subjects, both IS900 PCR and ELISA were performed. Although 11 were ELISA positive and 36 were PCR positive, in no instance was a patient positive by both tests, suggesting that these states are mutually exclusive. Evaluation of cytokine-mediated immune

responses of IBD patients was complicated by the influence of immunosuppressive therapy given most IBD patients. Gamma

\*\*\*interferon\*\*\* (IFN- gamma ) release by peripheral blood leukocytes after M. avium purified protein derivative PPD antigen stimulation showed significantly lower responses in CD patients than in UC patients or controls in both U.S. (by ex vivo \*\*\*assay\*\*\*\* ) and Danish (by in vitro

\*\*\*assay\*\*\* ) populations (P < 0.05). \*\*\*Interlewkin\*\*\* -5 responses were not different among CD, UC, or control groups. Collectively, the PCR, ELISA, and IFN- gamma tests for M. avium subsp. \*\*\*paratuberculosis\*\*\* together with the unexpected observation that BCG vaccination influenced M. avium subsp. \*\*\*paratuberculosis\*\*\* detection, lead us to conclude that M. avium subsp. \*\*\*paratuberculosis\*\*\*, or some similarly fastidious mycobacterial species, infects at least a subset of IBD patients. Whether the infection is primary (causal) or secondary, it may contribute to the etiopathogenesis of IBD.

I Results of Multiple \*\*\*Diagnostic\*\*\* Tests for Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* in Patients with Inflammatory Bowel Disease and in Controls

AB Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* has been incriminated as a cause of Crohn's disease (CD); however, studies to date have been relatively small and generally only used a single \*\*\*diagnostic\*\*\* \*\*\*assay\*\*\* . The objective of the study was to

reexamine the association of M. avium subsp. \*\*\*paratuberculosis\*\*\* and CD using multiple \*\*\*diagnostic\*\*\* tests. Five methods were used to detect Mavium subsp. \*\*\*paratuberculosis\*\*\* infections in 439 inflammatory bowel disease (IBD) patients and 324 control subjects in the United States and Denmark. Most \*\*\*assays\*\*\* were adaptations of \*\*\*diagnostic\*\*\* tests for this infection performed routinely on

\*\*\*diagnostic\*\*\* tests for this infection performed routinely on animals. PCR for IS900, a genetic element unique to M. avium subsp. \*\*\*paratuberculosis\*\*\* , was positive significantly more often on

resected bowel and lymph node tissues from CD patients (19.0%) and ulcerative colitis (UC). . . 0.02). Culture of the same tissues tested by PCR using modified BACTEC 12B medium failed to grow M. avium subsp.

\*\*\*aratuberculosis\*\*\* from patients or controls. U.S. CD patients had the highest serological evidence (enzyme-linked immunosorbent \*\*\*assay\*\*\* [ELISA] for serum antibodies) of M. avium subsp.

\*\*\*paratuberculosis\*\*\* infection (20.7% of patients positive) which was higher than for all UC patients studied (6.1%) or healthy controls (3.8%, P. . . of cytokine-mediated immune responses of IBD patients was complicated by the influence of immunosuppressive therapy given most IBD patients. Gamma \*\*\*interferon\*\* (IFN-gamma) release by peripheral blood leukocytes after M. avium purified protein derivative PPD antigen stimulation showed significantly lower responses in CD patients than in UC patients or controls in both U.S. (by ex vivo \*\*\*assay\*\*\*) and Danish (by in vitro \*\*\*assay\*\*\*) populations (P < 0.05). \*\*\*Interleukin\*\*\* -5 responses were not different among CD, UC, or control groups.

Collectively, the PCR, ELISA, and IFN- gamma tests for M. avium subsp.
\*\*\*paratuberculosis\*\*\* together with the unexpected observation that

vaccination influenced M. avium subsp. \*\*\*paratuberculosis\*\*\* detection, lead us to conclude that M. avium subsp.

BCG

\*\*\*paratuberculosis\*\*\* , or some similarly fastidious mycobacterial species, infects at least a subset of IBD patients. Whether the infection is primary (causal). . . .

UT Bactec test; BCG; Enzyme-linked immunosorbent \*\*\*assay\*\*\* ; Polymerase chain reaction; \*\*\*Diagnostic\*\*\* agents; Inflammatory bowel diseases; Crohn's disease; USA; Denmark; Mycobacterium avium

```
***paratuberculosis*** ; tests; man
```

- L10 ANSWER 17 OF 19 MEDLINE on STN
- AN 2001023445 MEDLINE <<LOGINID::20080325>>
- DN PubMed ID: 10895895
- TI Cytokine secretion by peripheral blood mononuclear cells from cows infected with Mycobacterium \*\*\*paratuberculosis\*\*\*
- AU Stabel J R
- CS Bacterial Diseases of Livestock Research Unit, USDA-Agricultural Research Services, National Animal Disease Center, Ames, IA 50010, USA.
- SO American journal of veterinary research, (2000 Jul) Vol. 61, No. 7, pp. 754-60.
- Journal code: 0375011. ISSN: 0002-9645.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 200011
- ED Entered STN: 22 Mar 2001 Last Updated on STN: 22 Mar 2001 Entered Medline: 3 Nov 2000
- AB OBJECTIVE: To compare cytokine secretion patterns of peripheral blood mononuclear cells (PBMC) from healthy cows and cows subclinically and clinically infected with Mycobacterium \*\*\*paratuberculosis\*\*\* .

  ANIMALS: 5 noninfected cows, 6 cows with subclinical
  - \*\*\*paratuberculosis\*\*\* , and 4 cows with clinical
  - \*\*\*paratuberculosis\*\*\* . PROCEDURE: PBMC were isolated, and concentrations or activities of secreted \*\*\*interleukin\*\*\* (IL)-1, IL-2, IL-6, tumor necrosis factor (TNF), and \*\*\*interferon\*\*\* -qamma (IFN-gamma) were measured after in vitro stimulation of cells with concanavalin A (ConA), lipopolysaccharide (LPS), or a whole-cell sonicate of M \*\*\*paratuberculosis\*\*\* (MpS). Proliferative responses of PBMC were also determined after stimulation with ConA, phytohemagglutinin, pokeweed mitogen (PWM), or MpS. RESULTS: After stimulation with ConA, cells from subclinically infected cows secreted significantly more, and cells from clinically infected cows secreted significantly less, IFN-gamma, compared with cells from control cows. Cells from cows with subclinical \*\*\*paratuberculosis\*\*\* produced significantly more TNF and IFN-gamma in response to MpS than cells from the other 2 groups. Stimulation of PBMC from subclinically infected cows with ConA or MpS resulted in significantly higher proliferative responses, compared with cells from control and clinically infected cows. In contrast, clinically infected cows had significantly higher proliferative responses to PWM than cells from the other 2 groups. CONCLUSIONS AND CLINICAL RELEVANCE: A decrease in T-cell responses to mitogens or MpS was observed in cows clinically infected with M \*\*\*paratuberculosis\*\*\* , compared with subclinically infected cows, suggesting that activated T cells may delay the progression of \*\*\*paratuberculosis\*\*\*
- TI Cytokine secretion by peripheral blood mononuclear cells from cows infected with Mycobacterium \*\*\*paratuberculosis\*\*\* .
- AB . . . cytokine secretion patterns of peripheral blood mononuclear cells (PBMC) from healthy cows and cows subclinically and clinically infected with Mycobacterium \*\*\*paratuberculosis\*\*\* . ANIMALS: 5 noninfected cows, 6 cows with subclinical \*\*\*paratuberculosis\*\*\* , and 4 cows with clinical \*\*\*paratuberculosis\*\*\* . PROCEDURE: PBMC were isolated, and concentrations or activities of secreted \*\*\*interleukin\*\*\* (IL)-1, IL-2, IU-6, tumor necrosis factor (TMF), and \*\*\*interfeorn\*\*\* -qamma

```
(IFN-gamma) were measured after in vitro stimulation of cells with
    concanavalin A (ConA), lipopolysaccharide (LPS), or a whole-cell sonicate
    of M ***paratuberculosis*** (MpS). Proliferative responses of PBMC
    were also determined after stimulation with ConA, phytohemagglutinin,
    pokeweed mitogen (PWM), or MpS. RESULTS: After. . . cells from
    clinically infected cows secreted significantly less, IFN-gamma, compared
    with cells from control cows. Cells from cows with subclinical
      ***paratuberculosis*** produced significantly more TNF and IFN-gamma in
    response to MpS than cells from the other 2 groups. Stimulation of PBMC.
     . . AND CLINICAL RELEVANCE: A decrease in T-cell responses to mitogens
    or MpS was observed in cows clinically infected with M
      ***paratuberculosis*** , compared with subclinically infected cows,
    suggesting that activated T cells may delay the progression of
       ***paratuberculosis***
*Cattle Diseases: IM, immunology
     Cattle Diseases: MI, microbiology
     Cell Division
     Concanavalin A: IM, immunology
     Cytokines: AN, analysis
    *Cvtokines: SE, secretion
        *** Enzyme-Linked Immunosorbent Assay: VE, veterinary***
        *** Interferon Type II: AN, analysis***
        *** Interleukin-1: AN, analysis***
        *** Interleukin-2: AN, analysis***
     Leukocytes, Mononuclear: IM, immunology
    *Leukocytes, Mononuclear: SE, secretion
     Lipopolysaccharides: IM, immunology
     Lymphocyte Activation
        ****Mycobacterium avium subsp. paratuberculosis: IM, immunology***
        *** Mycobacterium avium subsp. paratuberculosis: PY, pathogenicity***
        *** Paratuberculosis: BL, blood***
        ****Paratuberculosis: IM, immunology***
        *** Paratuberculosis: MI, microbiology***
     Phytohemagglutinins: IM, immunology
     Pokeweed Mitogens: IM, immunology
     Scintillation Counting: VE, veterinary
    11028-71-0 (Concanavalin A); ***82115-62-6 (Interferon Type II) ***
CN
    0 (Cvtokines); 0 ( ***Interleukin*** -1); 0 ( ***Interleukin*** -2); 0
    (Lipopolysaccharides); 0 (Phytohemagglutinins); 0 (Pokeweed Mitogens)
L10 ANSWER 18 OF 19
                        MEDLINE on STN
    1999314910
                  MEDLINE <<LOGINID::20080325>>
AN
DN
    PubMed ID: 10438314
       ***Interferon*** -gamma and ***interleukin*** -2 release by
    lymphocytes derived from the blood, mesenteric lymph nodes and intestines
    of normal sheep and those affected with ***paratuberculosis***
    (Johne's disease).
AU
    Burrells C; Clarke C J; Colston A; Kay J M; Porter J; Little D; Sharp J M
CS
   Moredun Research Institute, International Research Centre, Bush Loan,
    Penicuik, UK.. charles.burrells@cultor.com
SO
    Veterinary immunology and immunopathology, (1999 May) Vol. 68, No. 2-4,
    pp. 139-48.
    Journal code: 8002006, ISSN: 0165-2427,
    Netherlands
DT Journal: Article: (JOURNAL ARTICLE)
    (RESEARCH SUPPORT, NON-U.S. GOV'T)
```

TΙ

- LA English
- FS Priority Journals; AIDS
- EM 199908
- ED Entered STN: 16 Aug 1999
  - Last Updated on STN: 16 Aug 1999
  - Entered Medline: 3 Aug 1999
- This study sought to determine if T-cell cytokine responses to mycobacterial infections in sheep were similar to those in other species and if such responses correlated with prevailing gut pathology. Lymphocytes were isolated from the blood (PBL), mesenteric lymph nodes (MLN) and ileal lamina propria (LPL) of control sheep and of sheep with clinical Johne's disease due to infection with Mycobacterium avium ssp. \*\*\*paratuberculosis\*\*\* (M.a. \*\*\*paratuberculosis\*\*\* ). These

#### animals

had previously been categorised into two groups exhibiting either the 'tuberculoid' (paucibacillary) form of lesion or the 'lepromatous' (multibacillary) form. Lymphocytes were examined for their capacity, following stimulation with johnin-PPD, to release \*\*\*interferon\*\*\* -gamma (IFN-gamma) and \*\*\*interleukin\*\*\* 2 (IL-2) characteristic of the Th1 subset of MHC Class II-restricted CD4+ (helper) T-cells in other species. The expression of the two cytokines appeared related to the type of histological lesion observed. Antigen-stimulated lymphocytes from the tuberculoid group exhibited greater release of IFN-gamma and IL-2 than lymphocytes from the lepromatous group suggesting a Th1-type of response in the former in which expression of IFN-gamma by PBL showed a significant positive correlation with that expressed by MLN and LPL. Lymphocytes from animals with lepromatous lesions released lesser mycobacterium-induced IFN-gamma and IL-2 indicating a diminished role for a Th1 subset in this group of sheep. Differences in cytokine expression were much more apparent with lymphocytes which were derived from MLN.

- \*\*\*Interferon\*\*\* -qamma and \*\*\*interleukin\*\*\* -2 release by lymphocytes derived from the blood, mesenteric lymph nodes and intestines of normal sheep and those affected with \*\*\*paratuberculosis\*\*\* (Johne's disease).
- AB . . . lamina propria (LPL) of control sheep and of sheep with clinical Johne's disease due to infection with Mycobacterium avium ssp. \*\*\*paratuberculosis\*\*\* (M.a. \*\*\*paratuberculosis\*\*\* ). These

## animals

had previously been categorised into two groups exhibiting either the 'tuberculoid' (paucibacillary) form of lesion or the 'lepromatous' (multibacillary) form. Lymphocytes were examined for their capacity, following stimulation with johnin-PPD, to release \*\*\*interferon\*\*\* -gamma (IFN-gamma) and \*\*\*interleukin\*\*\* 2 (IL-2) characteristic of the Th1 subset of MHC Class II-restricted CD4+ (helper) T-cells in other species. The expression of. . .

Check Tags: Female

Animals

```
*** Enzyme-Linked Immunosorbent Assay: VE, veterinary***
Ileum
   ****Interferon Type II: BI, biosynthesis***
   ****Interleukin-2: BI, biosynthesis***
Lymph Nodes: CY, cytology
*Lymph Nodes: ME, metabolism
Lymphocyte Activation
Mesentery
   ****Paratuberculosis: ME, metabolism***
Sheep
```

- \*Sheep Diseases: ME, metabolism
- \*Th1 Cells: ME, metabolism
- RN \*\*\*82115-62-6 (Interferon Type II) \*\*\*
- CN 0 ( \*\*\*Interleukin\*\*\* -2)
- L10 ANSWER 19 OF 19 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 7
- AN 1998:363991 BIOSIS <<LOGINID::20080325>>
- DN PREV199800363991
- TI \*\*\*Interferon\*\*\* -gamma and \*\*\*interleukin\*\*\* 4 gene expression in cows infected with Mycobacterium \*\*\*paratuberculosis\*\*\* .
- AU Sweeney, Raymond W. [Reprint author]; Jones, Douglas E.; Habecker, Perry; Scott, Phillip
- CS Dep. Clinical Studies-New Bolton Cent., Sch. Veterinary Med., Univ.
- Pennsylvania, 382 W. Street Rd., Kennett Square, PA 19348, USA SO American Journal of Veterinary Research, (July, 1998) Vol. 59, No. 7, pp.
- 842-847. print. CODEN: AJVRAH. ISSN: 0002-9645.
- DT Article
- LA English
- ED Entered STN: 27 Aug 1998
- Last Updated on STN: 27 Aug 1998
- AB Objective-To determine whether clinical progression of \*\*\*paratuberculosis\*\*\* in cattle was associated with alterations in
  - cytokine gene expression in affected tissues. Animals-5 uninfected adult Holstein cows, 7 adult Holstein cows naturally infected with Mycobacterium \*\*\*paratuberculosis\*\*\* that did not have clinical signs of disease, and 4 adult Holstein cows naturally infected with M. \*\*\*paratuberculosis\*\*\* that had progressive clinical signs of infection. Procedure-Samples of ileum and cecal lymoh nodes were obtained from each animal at the time of
  - that had progressive clinical signs of infection. Procedure-Samples or ileum and cecal lymph nodes were obtained from each animal at the time of slaughter. A reverse transcriptase-competitive polymerase chain reaction \*\*\*assay\*\*\* was used to determine mRNA expression of \*\*\*interferon\*\*\* -qamma (IFN-qamma) and \*\*\*interleukin\*\*\* 4 in each sample. Results-
  - \*\*\*Interferon\*\*\* -gamma gene expression was significantly higher in

# ileum

- and cecal lymph node samples from subclinically infected cows than from clinically infected cows. Conclusions and Clinical Relevance-Progression of \*\*\*paratuberculosis\*\*\* to clinical stages is associated with reduced expression of IFN-gamma at site of infection. If immune response to M. \*\*\*paratuberculosis\*\*\* can be manipulated so that IFN-gamma expression is increased, resistance to infection in cattle might be enhanced.
- TI \*\*\*Interferon\*\*\* -gamma and \*\*\*interleukin\*\*\* 4 gene expression in cows infected with Mycobacterium \*\*\*paratuberculosis\*\*\* .
- AB Objective-To determine whether clinical progression of
  - \*\*\*paratuberculosis\*\*\* in cattle was associated with alterations in cytokine gene expression in affected tissues. Animals-5 uninfected adult Holstein cows, 7 adult Holstein cows naturally infected with Mycobacterium
    - \*\*\*paratuberculosis\*\*\* that did not have clinical signs of disease, and a adult Holstein cows naturally infected with M. \*\*\*paratuberculosis\*\*\* that had progressive clinical signs of infection. Procedure-Samples of ileum and cecal lymph nodes were obtained from each animal at the time of slaughter. A reverse transcriptase-competitive polymerase chain reaction \*\*\*assay\*\*\* was used to determine mRNA expression of \*\*\*interferon\*\*\*
    - -gamma (IFN-gamma) and \*\*\*interleukin\*\*\* 4 in each sample. Results\*\*\*Interferon\*\*\* -gamma gene expression was significantly higher in

and cecal lymph node samples from subclinically infected cows than from clinically infected cows. Conclusions and Clinical Relevance-Progression of \*\*\*paratuberculosis\*\*\* to clinical stages is associated with reduced expression of IFN-gamma at site of infection. If immune response \*\*\*paratuberculosis\*\*\* can be manipulated so that IFN-gamma expression is increased, resistance to infection in cattle might be enhanced. Major Concepts Immune System (Chemical Coordination and Homeostasis); Infection; Veterinary Medicine (Medical Sciences) Diseases Mycobacterium- \*\*\*paratuberculosis\*\*\* infection: bacterial disease Mycobacterium Infections (MeSH) Chemicals & Biochemicals \*\*\*interferon\*\*\* -qamma: gene expression; \*\*\*interleukin\*\*\* -4: gene expression ORGN . Vertebrates, Nonhuman Mammals, Vertebrates ORGN Classifier Mycobacteriaceae 08881 Super Taxa Mycobacteria; Actinomycetes and Related Organisms; Eubacteria; Bacteria: Microorganisms Organism Name Mycobacterium- \*\*\*paratuberculosis\*\*\* : pathogen Taxa Notes Bacteria, Eubacteria, Microorganisms => s 110 and (interleukin 10) 7 L10 AND (INTERLEUKIN 10) => d 1-YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):v L11 ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN 2006:496945 BIOSIS <<LOGINID::20080325>> PREV200600503265 Disturbed cytokine response to mycobacterium avium subspecies \*\*\*paratuberculosis\*\*\* is dysregulated in patients with Crohn's disease. Sibartie, Shomik; Keohane, John; Scully, Paul; O'Neill, Shaun; O'Mahony, Jim; O'Mahony, Liam; Shanahan, Fergus Gastroenterology, (APR 2006) Vol. 130, No. 4, Suppl. 2, pp. A240. Meeting Info.: Digestive Disease Week Meeting/107th Annual Meeting of the American-Gastroenterological-Association. Los Angeles, CA, USA. May 19 -24, 2006. Amer Gastroenterol Assoc Inst. CODEN: GASTAB. ISSN: 0016-5085. Conference; (Meeting) Conference; Abstract; (Meeting Abstract) English Entered STN: 4 Oct 2006 Last Updated on STN: 4 Oct 2006

L11 ANSWER 2 OF 7 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2004:178760 BIOSIS <<LOGINID::20080325>> DN PREV200400179647

TT

ΙT

AN

DN

AU

ED

- Cytokine gene expression in peripheral blood mononuclear cells and tissues of cattle infected with Mycobacterium avium subsp.
  - \*\*\*paratuberculosis\*\*\* : Evidence for an inherent proinflammatory gene expression pattern.
- Coussens, Paul M. [Reprint Author]; Verman, Nitin; Coussens, Marc A.; AII Elftman, Michael D.; McNulty, Amanda M.
- Department of Animal Science, Michigan State University, 1205H Anthony Hall, East Lansing, MI, 48824, USA coussens@msu.edu
- Infection and Immunity, (March 2004) Vol. 72, No. 3, pp. 1409-1422. print. ISSN: 0019-9567 (ISSN print).
- DT Article
- LA English
- Entered STN: 31 Mar 2004 ED
- Last Updated on STN: 31 Mar 2004
- L11 ANSWER 3 OF 7 CABA COPYRIGHT 2008 CABI on STN
- AN 2006:49179 CABA <<LOGINID::20080325>>
- DN 20063031176
- ΤI Inflammatory cytokine gene expression in different types of granulomatous lesions during asymptomatic stages of bovine \*\*\*paratuberculosis\*\*\*
- AU Tanaka, S.; Sato, M.; Onitsuka, T.; Kamata, H.; Yokomizo, Y.
- CS Comparative Pathology Section, Kyushu Research Station, National Institute of Animal Health, Chuzan-cho 2702, Kagoshima 891-0105, Japan. tanakas@affrc.go.jp
- Veterinary Pathology, (2005) Vol. 42, No. 5, pp. 579-588. 41 ref. SO Publisher: American College of Veterinary Pathologists Inc. Lawrence ISSN: 0300-9858 DOI: 10.1354/vp.42-5-579
- CY United States
- DT Journal
- LΑ English
- ED Entered STN: 2 Mar 2006 Last Updated on STN: 2 Mar 2006
- L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
- 2007:906779 CAPLUS <<LOGINID::20080325>> AN
- DN 147:275692
- TI Sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in the early stages and paucibacillary infections
- IN Ottenhof, Tom Henricus Maria; Geluk, Annemieke; Pereira Sampaio, Elizabeth
- PA Leiden University Medical Center, Neth.
- SO PCT Int. Appl., 70pp.
- CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

	PA:	TENT	NO.			KIN	D	DATE			APPLICATION NO.						DATE			
PI	WO 2007091881					A2	2 20070816				WO 2006-NL50105						20060428			
	WO 2007091881					A3	A3 20071129													
		W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,		
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,		
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KN,	KP,	KR,		

KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,

```
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZM

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GM, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI EP 2005-103576

A 20050429
```

- L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2004:885718 CAPLUS <<LOGINID::20080325>>
- DN 141:363746
- TI Development of early-stage \*\*\*diagnostic\*\*\* method for Johne disease by using anti-IL-10 antibody
- AU Momotani, Eiichi; Mori, Yasuyuki
- CS Natl. Agric. Bio-oriented Res. Org., Natl. Inst. Animal Health, Tsukuba, 305-0856, Japan
- SO BRAIN Techno News (2004), 105, 18-24
- CODEN: BTEEEC; ISSN: 1345-5958
- PB Nogyo, Seibutsukei Tokutei Sangyo Gijutsu Kenkyu Kiko, Seibutsukei Tokutei Sangyo Gijutsu Kenkyu Shien Senta
- DT Journal; General Review
- LA Japanese
- L11 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2003:472526 CAPLUS <<LOGINID::20080325>>
- DN 139:30816
- TI Peptide T and analogs thereof for the stimulation of cytotoxic T lymphocyte (CTL) responses and increasing secretion of \*\*\*interferon\*\*\* .camma. and \*\*\*interleukin\*\*\* 2, and therapeutic use
- IN Ruscetti, Francis W.; Ruff, Michael R.
- PA The Government of the United States of America, as Represented by the Secretary Department of Health and Human Services National Institutes of Health, USA
- SO PCT Int. Appl., 43 pp.

OS MARPAT 139:30816

- CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

	PA:	TENT :	NO.		KIND		DATE		APPLICATION NO.						DATE				
PI	WO	O 2003050136						20030619		WO 2002-US39109						20021206			
	WO	2003	A3		20031204														
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
			CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
			GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	
			PL,	PT,	RO,	RU,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	
			UG,	US,	UZ,	VN,	YU,	ZA,	ZM,	zw									
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,	
			KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	
			FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	SI,	SK,	TR,	BF,	BJ,	
			CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
	AU	AU 2002357093				A1		2003	0623	AU 2002-357093						20021206			
PRAI	US 2001-338971P			P		2001	1207												
	WO 2002-US39109					W		2002	1206										

```
L11 ANSWER 7 OF 7 MEDLINE on STN
    2007416292 MEDLINE <<LOGINID::20080325>>
AN
DN
    PubMed ID: 17502388
TI Influence of Mycobacterium avium subsp. ***paratuberculosis*** on
    colitis development and specific immune responses during disease.
AU
    Singh Udai P; Singh Shailesh; Singh Rajesh; Karls Russell K; Quinn
    Frederick D; Potter Morris E; Lillard James W Jr
    Brown Cancer Center, Department of Microbiology and Immunology, University
CS
    of Louisville, 580 S. Preston Street, Baxter II/Room 304C, Louisville, KY
    40202, USA.
    AI 57808 (United States NIAID)
NC
    GM 08248 (United States NIGMS)
    MD 000525 (United States NCMHD)
    RR 03034 (United States NCRR)
    Infection and immunity, (2007 Aug) Vol. 75, No. 8, pp. 3722-8. Electronic
     Publication: 2007-05-14.
    Journal code: 0246127. ISSN: 0019-9567.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
    (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS
   Priority Journals
EM
    200709
ED Entered STN: 20 Jul 2007
    Last Updated on STN: 7 Sep 2007
    Entered Medline: 6 Sep 2007
=> s 111 and (anti-interleukin)
L12
           0 L11 AND (ANTI-INTERLEUKIN)
=> s 111 and (antibody to interleukin)
L13
            0 L11 AND (ANTIBODY TO INTERLEUKIN)
=> s 111 and ((antibody)2w(interleukin))
MISSING OPERATOR ANTIBODY) 2W
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.
=> s 111 and (antibody(2w)interleukin)
L14
            0 L11 AND (ANTIBODY(2W) INTERLEUKIN)
=> d kwic 111 1-
YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):v
L11 ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Disturbed cytokine response to mycobacterium avium subspecies
      ***paratuberculosis*** is dysregulated in patients with Crohn's
disease.
    Background: Mycobacterium avium subspecies ***paratuberculosis***
     (MAP) has been a source of controversy since it was first suggested as a
    possible cause for Crohn's disease. While. . . few studies have
    examined the cellular immune response to MAP. Aim: To compare the
    cellular response to Mycobacterium avium subspecies
```

\*\*\*paratuberculosis\*\*\* between Crohn's disease patients and healthy

```
volunteers. Methods: Peripheral blood mononuclear cells (PBMCs) were
    isolated from 24 Crohn's disease patients. . .
    . . .
       system, blood and lymphatics, PBMC; phagocytic cell: immune system
    Diseases
       Crohn's disease: digestive system disease, immune system disease,
       etiology, ***diagnosis***
TT
    Chemicals & Biochemicals
       cytokines; IFN-gamma [ ***interferon*** -gamma]; IL-10 [
          ***interleukin*** - ***10*** ]; TNF-alpha [tumor necrosis
       factor-alpha]; IL-6 [ ***interleukin*** -6]; IL-8 [
         ***interleukin*** -8]; IL-2 [ ***interleukin*** -2]; IL-4 [
         ***interleukin*** -4]
       Primates, Vertebrates
ORGN Classifier
       Mycobacteriaceae 08881
    Super Taxa
       Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
       Bacteria; Microorganisms
    Organism Name
       Mycobacterium avium ***paratuberculosis*** (subspecies): pathogen
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
L11 ANSWER 2 OF 7 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
```

- Cytokine gene expression in peripheral blood mononuclear cells and tissues of cattle infected with Mycobacterium avium subsp.
  - \*\*\*paratuberculosis\*\*\* : Evidence for an inherent proinflammatory gene expression pattern.
  - In cattle and other ruminants, infection with the intracellular pathogen Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\* results in a granulomatous enteritis (Johne's disease) that is often fatal. The key features of host immunity to M. avium subsp. \*\*\*paratuberculosis\*\*\* infection include an appropriate early proinflammatory and cytotoxic response (Th1-like) that eventually gives way to a predominant antibody-based response (Th2-like) .. . this shift in the immune response occurs and the underlying molecular mechanisms involved is critical to future control measures and \*\*\*diagnosis\*\*\* . Previous studies have suggested that M. avium subsp. \*\*\*paratuberculosis\*\*\* may suppress dene expression in peripheral blood mononuclear cells (PBMCs) from infected cows, despite a continued inflammatory reaction at sites of infection. In the present study, we tested the hypothesis that exposure to M. avium subsp. \*\*\*paratuberculosis\*\*\* suppresses a proinflammatory gene expression pattern in PBMCs from infected cows. To do this, we examined expression of genes encoding \*\*\*interleukin\*\*\* -lalpha (IL-lalpha), IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p35, IL-16, and IL-18, as well as genes encoding gamma \*\*\*interferon\*\*\* (IFN-gamma), transforming growth factor beta (TGF-beta), and tumor necrosis factor alpha (TNF-alpha), in PBMCs, intestinal lesions, and mesenteric lymph nodes of cattle naturally infected with M. avium subsp.
    - \*\*\*paratuberculosis\*\*\* . Cytokine gene expression in these cells and tissues was compared to expression in similar cells and tissues from control uninfected. . . IL-8, and IL-12p35, differential expression in PBMCs from infected and control cattle did not require stimulation with M. avium subsp. \*\*\*paratuberculosis\*\*\* . In fact, stimulation with M. avium subsp. \*\*\*paratuberculosis\*\*\* tended to reduce the differential

```
expression observed in infected and uninfected cows for genes encoding
    IFN-gamma, IL-lalpha, and IL-6. Only IL-10 gene expression was
    consistently enhanced by M. avium subsp. ***paratuberculosis***
    stimulation of PBMCs from subclinically infected cattle. In ileal tissues
    from M. avium subsp. ***paratuberculosis*** -infected cattle,
    expression of the genes encoding IFN-gamma, TGF-beta, IL-5, and IL-8 was
    greater than the expression in comparable tissues from. . . was lower
    in tissues from infected cattle than in control tissues. Mesenteric lymph
    nodes draining sites of M. avium subsp. ***paratuberculosis***
    infection expressed higher levels of IL-lalpha, IL-8, IL-2, and IL-10 mRNA
    than similar tissues from control uninfected cattle expressed. In. .
    cattle. Taken together, our results suggest that cells or other
    mechanisms capable of limiting proinflammatory responses to M. avium
    subsp. ***paratuberculosis*** develop in infected cattle and that a
    likely place for development and expansion of these cell populations is
    the mesenteric. . .
   . . .
       lymph node: blood and lymphatics, digestive system, immune system;
       peripheral blood mononuclear cell: blood and lymphatics, immune system
           ***paratuberculosis*** : bacterial disease, infectious disease,
       genetics, immunology, Johne's disease
           ***Paratuberculosis***
                                  (MeSH)
    Chemicals & Biochemicals
       proinflammatory genes: expression pattern
ORGN .
       Vertebrates
ORGN Classifier
       Mycobacteriaceae 08881
    Super Taxa
       Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
       Bacteria; Microorganisms
    Organism Name
       Mycobacterium avium ssp. ***paratuberculosis*** (subspecies):
       pathogen
    Taxa Notes
       Bacteria, Eubacteria, Microorganisms
GEN cattle IFN-gamma gene [cattle ***interferon*** -gamma gene] (Bovidae);
    cattle IL-1-alpha gene [cattle ***interleukin*** -1-alpha gene]
    (Bovidae); cattle IL-10 gene [cattle ***interleukin*** - ***10***
    gene] (Bovidae); cattle IL-12p35 gene [cattle ***interleukin*** -12p35
    gene] (Bovidae); cattle IL-16 gene [cattle ***interleukin*** -16 gene]
    (Bovidae); cattle IL-18 gene [cattle ***interleukin*** -18 gene]
    (Bovidae); cattle IL-2 gene [cattle ***interleukin*** -2 gene]
    (Bovidae); cattle IL-4 gene [cattle ***interleukin*** -4 gene]
    (Bovidae); cattle IL-5 gene [cattle ***interleukin*** -5 gene]
    (Bovidae); cattle IL-6 gene [cattle ***interleukin*** -6 gene]
    (Bovidae); cattle IL-8 gene [cattle ***interleukin*** -8 gene]
    (Bovidae); cattle TGF-beta gene [cattle transforming growth factor-beta
    gene] (Bovidae); cattle TNF-alpha gene [cattle tumor necrosis factor-alpha
    gene] (Bovidae)
```

- L11 ANSWER 3 OF 7 CABA COPYRIGHT 2008 CABI on STN
- TI Inflammatory cytokine gene expression in different types of granulomatous lesions during asymptomatic stages of bovine \*\*\*paratuberculosis\*\*\* . AB The granulomatous lesions in bovine \*\*\*paratuberculosis\*\*\* have been classified into two types, i.e., the lepromatous type and the tuberculoid

```
type. To clarify the immunopathologic mechanisms at. . . the two types of lesions. Samples were obtained from noninfected control cows (n=5) and naturally infected cows (n=7) that were ***diagnosed*** by enzyme-linked immunosorbent ***asay*** (ELISA) and faecal culture test. Although none of the infected cows showed clinical signs, tuberculoid lesions were observed in five. . and lepromatous lesions in two cows (lepromatous group). Among the cytokines examined by reverse transcription-polymerase chain reaction (RT-PCR), Th2-type cytokines ***interleuki*** -4 (IL-4) and IL-10, and Th1-type cytokine IL-2 were expressed more significantly in the lepromatous group than in the tuberculoid (Pc0.01) and noninfected groups (Pc0.05). No statistical differences were observed in the expression of ***interferent** -qamma,
```

expressed more significantly in the lepromatous group than in the tuberculoid (Pc0.01) and noninfected groups (Pc0.05). No statistical differences were observed in the expression of \*\*\*interferon\*\*\* -gamma, IL-1 beta, TNF-alpha, and GM-CSF among lepromatous, tuberculoid, and noninfected groups. Expression of proinflammatory cytokine IL-12 mRNA, however, did not. . . influenced by alterations in Th1/Th2-type cytokine production and that IL-18 may play an important role in a Th1-to-Th2 switch in \*\*\*paratuberculosis\*\*\*.

CT cows; cytokines; disease course; gene expression; genes; granuloma; histopathology; immunopathology; \*\*interferon\*\*\*; \*\*\*interleukin\*\*\* 2; \*\*\*interleukin\*\*\* 4; \*\*\*interleukins\*\*\*; messenger RNA; \*\*\*paratuberculosis\*\*\*; tumour necrosis factor

ST \*\*\*interleukin\*\*\* 18

ORGN cattle; Mycobacterium avium subsp. \*\*\*paratuberculosis\*\*\*

- L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in the early stages and paucibacillary infections
- AB The current invention discloses new Mycobacterium leprae antigens to be used in methods and means for detection and \*\*\*diagnostics\*\*\* of M. leprae infections in subjects, in particular in the early stages of infection and in paucibacillary infections, which remain undetected using conventional \*\*\*diagnostic\*\*\* methods. The antigens disclosed in the invention are specific for M. leprae and the \*\*\*diagnostic\*\*\* method does not yield 'false pos.' results in individuals having an immune response against other Mycobacterial species, such as M. tuberculosis, M. bovis, M. \*\*\*paratuberculosis\*\*\* , M. avium, M. smegmatis, , M. ulcerans, M. microti, and M. marinum, or BCG vaccinated individuals. Thus, using bioinformatic anal. the. . . in human leprosy tissue. Paucibacillary and reactional leprosy patients and healthy household contacts of leprosy patients produced significant levels of \*\*\*interferon\*\*\* (IFN)-.gamma. in response to the five unique M. leprae antigens encoded by ML0576, ML1989, ML1990, ML2283 and ML2567. Provided are. . .
- ST sequence Mycobacterium leprae antigen epitope \*\*\*diagnoses\*\*\*
  infection; leprosy immunodiagnosis Mycobacterium leprae antigen epitope;
  vaccine Mycobacterium leprae antigen epitope
- IT Receptors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study) (4-1BB, anti-4-1BB agonistic antibody as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections!
- IT Human groups

(Brazilian patients; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae,

```
leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
        paucibacillary infections)
ΤТ
     Histocompatibility antigens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (HLA, class I, identifying T-cell epitopes for, using computer
        algorithms; sequences for Mycobacterium leprae-specific antigens, and
       methods for treating and ***diagnosing*** M. leprae, particularly
        in early stages and paucibacillary infections)
ΙT
     Histocompatibility antigens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (HLA, class II, identifying T-cell epitopes for, using computer
        algorithms; sequences for Mycobacterium leprae-specific antigens, and
                                 ***diagnosing*** M. leprae, particularly
       methods for treating and
        in early stages and paucibacillary infections)
     Proteins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (LAG3 (lymphocyte activation gene-3), sol., as adjuvant; sequences for
        Mycobacterium leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
        paucibacillary infections)
    Gene, microbial
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); PRP (Properties); BIOL (Biological study)
        (ML0573, expressed in human leprosy tissue; sequences for Mycobacterium
        leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
        paucibacillary infections)
     Gene, microbial
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); PRP (Properties); BIOL (Biological study)
        (ML0574, expressed in human leprosy tissue; sequences for Mycobacterium
        leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
        paucibacillary infections)
     Gene, microbial
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); PRP (Properties); BIOL (Biological study)
        (ML0575, expressed in human leprosy tissue; sequences for Mycobacterium
        leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
        paucibacillary infections)
    Gene, microbial
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); PRP (Properties); BIOL (Biological study)
        (ML0576, expressed in human leprosy tissue; sequences for Mycobacterium
        leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
```

RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL

particularly in early stages and paucibacillary infections)

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (CpG island, CpG, as adjuvant; sequences for Mycobacterium

IΤ

Genetic element

Antigens

```
(Biological study); USES (Uses)
        (ML0576; sequences for Mycobacterium leprae-specific antigens, and
        methods for treating and ***diagnosing*** M. leprae, particularly
        in early stages and paucibacillary infections)
     Gene, microbial
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); PRP (Properties); BIOL (Biological study)
        (ML1602, expressed in human leprosy tissue; sequences for Mycobacterium
        leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
        paucibacillary infections)
ΙT
     Gene, microbial
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); PRP (Properties); BIOL (Biological study)
        (ML1603, expressed in human leprosy tissue; sequences for Mycobacterium
        leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
```

# paucibacillary infections) IT Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML1604, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

#### IT Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML1788, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and

paucibacillary infections)

## IT Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML1989, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

#### T Antigens

RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(ML1989; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

# Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML1990, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and

paucibacillary infections)

### T Antigens

RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use);

PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (ML1990; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stades and paucibacillary infections)

IT Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ML2283, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and

paucibacillary infections)

IT Antigens

RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(ML2283; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Gene, microbial

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (ML2567, expressed in human leprosy tissue; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Antigens

RL: ADV (Adverse effect, including toxicity); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(ML2567; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Lipopeptides

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Pam3Cys, as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Immunostimulants

(adjuvants, DA/TDB; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Immunostimulants

(adjuvants, DDA/MPL; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Immunostimulants

(adjuvants; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

IT Monocyte

(anal., in \*\*\*diagnosis\*\*\*; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

```
***Diagnostic*** agents
    Vaccines
       (antigens or epitopes as; sequences for Mycobacterium leprae-specific
       antigens, and methods for treating and ***diagnosing*** M. leprae,
       particularly in early stages and paucibacillary infections)
   Lipid A
    Lipopolysaccharides
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
       (as adjuvant; sequences for Mycobacterium leprae-specific antigens, and
       methods for treating and ***diagnosing*** M. leprae, particularly
       in early stages and paucibacillary infections)
ΙT
    Mycobacterium
        (as recombinant expression host; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
ΤТ
    Flagellins
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (bacterial, as adjuvant; sequences for Mycobacterium leprae-specific
       antigens, and methods for treating and ***diagnosing*** M. leprae,
       particularly in early stages and paucibacillary infections)
ΙT
    CD40 (antigen)
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (binding CD40 ligand or antibody, as adjuvant; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    Mammalia
TT
       ( ***diagnosis*** and therapy; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    Mycobacterium avium
    Mycobacterium bovis
    Mycobacterium marinum
    Mycobacterium microti
    Mycobacterium smegmatis
    Mycobacterium tuberculosis
    Mycobacterium ulcerans
       (differentiating from; sequences for Mycobacterium leprae-specific
       antigens, and methods for treating and ***diagnosing*** M. leprae,
       particularly in early stages and paucibacillary infections)
TT
   Leprosv
        (early stages
                      ***diagnosis*** ; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    T cell (lymphocyte)
        (epitopes; sequences for Mycobacterium leprae-specific antigens, and
       methods for treating and ***diagnosing*** M. leprae, particularly
       in early stages and paucibacillary infections)
ΙT
    Epitopes
       (from ML0576, ML1989, ML1990, ML2283 and ML2567 antigens; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    T cell (lymphocyte)
```

(helper cell, measuring response, in \*\*\*diagnosis\*\*\* ; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) Algorithm (identifying HLA class I and/or class II T-cell epitopes using; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) \*\*\*Diagnosis\*\*\* (immunodiagnosis, of ML0576, ML1989, ML1990, ML2283 and ML2567 antigens; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) Blood analysis (in \*\*\*diagnosis\*\*\* ; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) \*\*\*Interleukin\*\*\* \*\*\*10\*\*\* \*\*\*Interleukin\*\*\* 15 \*\*\*Interleukin\*\*\* 2 \*\*\*Interleukin\*\*\* 4 \*\*\*Interleukin\*\*\* 6 Macrophage inflammatory protein 1.beta. Transforming growth factor .beta. Tumor necrosis factors RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (measuring response, in \*\*\*diagnosis\*\*\* ; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) Antibodies and Immunoglobulins RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (monoclonal, anti-4-1BB, agonistic, as adjuvant; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections) Genome

TT

ΤТ

TТ

ΙT

ΙT

ΤТ

(of M. leprae, identifying unique antigen gene candidates in; sequences for Mycobacterium leprae-specific antigens, and methods for treating \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and

paucibacillary infections)

Protein sequences (of M. leprae-specific antigens ML0576, ML1989, ML1990, ML2283 and ML2567; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

ΙT DNA sequences

(of M. leprae-specific genes ML0576, ML1989, ML1990, ML2283 and ML2567; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and paucibacillary infections)

TT Blood cell

> (of infected subject, IFN-.gamma. response in; sequences for Mycobacterium leprae-specific antigens, and methods for treating and \*\*\*diagnosing\*\*\* M. leprae, particularly in early stages and

```
unclassified); ANST (Analytical study); BIOL (Biological study)
        (p70, measuring response, in ***diagnosis*** ; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
ΙT
    Human
       (patients; sequences for Mycobacterium leprae-specific antigens, and
       methods for treating and ***diagnosing*** M. leprae, particularly
       in early stages and paucibacillary infections)
IT
    Infection
                         ***diagnosis*** ; sequences for Mycobacterium
       (paucibacillary,
       leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
ΙT
    Bioinformatics
        (sequence annotation, M. leprae unique genes; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
ΙT
    Molecular cloning
    Mycobacterium leprae
    Test kits
       (sequences for Mycobacterium leprae-specific antigens, and methods for
       treating and
                     ***diagnosing*** M. leprae, particularly in early
       stages and paucibacillary infections)
ΙT
        (test, by applying antigen under top skin; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
          ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
ΙT
    Mycobacterium BCG
        (vaccine, differentiating from; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
тт
       ***Interferons***
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); ANST (Analytical study); BIOL (Biological study)
        (.alpha., measuring response, in ***diagnosis***; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
       ***Interferons***
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); ANST (Analytical study); BIOL (Biological study)
        (.beta., measuring response, in ***diagnosis*** ; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
      ***Interferons***
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); ANST (Analytical study); BIOL (Biological study)
        (.gamma., measuring response, in ***diagnosis*** ; sequences for
```

Mycobacterium leprae-specific antigens, and methods for treating and

RL: ARU (Analytical role, unclassified); BSU (Biological study,

paucibacillary infections)

\*\*\*Interleukin\*\*\* 12

ΙT

```
***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    141256-04-4, OS21
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (MPL, as adjuvant; sequences for Mycobacterium leprae-specific
       antigens, and methods for treating and ***diagnosing*** M. leprae,
       particularly in early stages and paucibacillary infections)
ΤТ
    946442-88-2 946442-91-7
    RL: PRP (Properties)
       (Unclaimed; sequences for Mycobacterium leprae-specific antigens, and
       methods for treating and ***diagnosing*** M. leprae, particularly
       in the early stages and paucibacillary infections)
    946400-78-8 946400-79-9 946400-80-2 946400-81-3
                                                           946400-82-4
    RL: ADV (Adverse effect, including toxicity); ARU (Analytical role,
    unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use);
    PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
    (Biological study); USES (Uses)
        (amino acid sequence, epitope; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    946442-52-0 946442-53-1 946442-54-2 946442-55-3 946442-56-4
    RL: ADV (Adverse effect, including toxicity); ARU (Analytical role,
    unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use);
    PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); USES (Uses)
        (amino acid sequence; sequences for Mycobacterium leprae-specific
       antigens, and methods for treating and ***diagnosing*** M. leprae,
       particularly in early stages and paucibacillary infections)
TТ
    24939-03-5, Polv(I:C) 87420-41-5, Pam3Cvs 911642-39-2, IC 31
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
       (as adjuvant; sequences for Mycobacterium leprae-specific antigens, and
       methods for treating and ***diagnosing*** M. leprae, particularly
       in early stages and paucibacillary infections)
    83869-56-1, GM-CSF
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); ANST (Analytical study); BIOL (Biological study)
        (measuring response, in ***diagnosis*** ; sequences for
       Mycobacterium leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in early stages and
       paucibacillary infections)
    946442-57-5, DNA (Mycobacterium leprae gene ML0576) 946442-58-6, DNA
    (Mycobacterium leprae gene ML1989) 946442-59-7, DNA (Mycobacterium
    leprae gene ML1990) 946442-60-0, DNA (Mycobacterium leprae gene ML2283)
    946442-61-1, DNA (Mycobacterium leprae gene ML2567)
    RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
    unclassified); PRP (Properties); BIOL (Biological study)
       (nucleotide sequence; sequences for Mycobacterium leprae-specific
       antigens, and methods for treating and ***diagnosing*** M. leprae,
       particularly in early stages and paucibacillary infections)
    946442-98-4 946442-99-5 946443-00-1 946443-01-2 946443-02-3
    946443-03-4 946443-04-5 946443-05-6 946443-06-7 946443-07-8
    946443-08-9 946443-09-0
    RL: PRP (Properties)
```

(unclaimed nucleotide sequence; sequences for Mycobacterium leprae-specific antigens, and methods for treating and

\*\*\*diagnosing\*\*\* M. leprae, particularly in the early stages and

```
paucibacillary infections)
   946442-86-0 946442-87-1 946442-89-3 946442-90-6 946442-92-8
IT
    946442-93-9 946442-94-0 946442-95-1 946442-96-2 946442-97-3
    RL: PRP (Properties)
       (unclaimed protein sequence; sequences for Mycobacterium
       leprae-specific antigens, and methods for treating and
         ***diagnosing*** M. leprae, particularly in the early stages and
       paucibacillary infections)
L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
    Development of early-stage
                               ***diagnostic*** method for Johne disease
    by using anti-IL-10 antibody
AB
    A review on early-stage ***diagnosis*** of Johne's disease (
      ***paratuberculosis*** ) in cattle by modified ***interferon***
    .gamma. ELISA ***assay*** using IL-10 neutralizing antibody, and its
    effectiveness.
   review cattle Johne disease ***diagnosis*** ELISA ***interleukin***
      ***10*** antibody; ***paratuberculosis*** cattle ***diagnosis***
      ***interferon*** gamma ELISA review
    Mycobacterium avium ***paratuberculosis***
       (early-stage ***diagnosis*** method for Johne's disease using
       anti-IL-10 antibody)
                           ***10***
      ***Interleukin***
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
       (early-stage ***diagnosis*** method for Johne's disease using
       anti-IL-10 antibody)
TТ
    Immunoassav
       (enzyme-liked immunosorbent ***assay*** ; early-stage
         ***diagnosis*** method for Johne's disease using anti-IL-10
antibody)
ΙT
       ***Diagnosis***
       (immunodiagnosis; early-stage ***diagnosis*** method for Johne's
       disease using anti-IL-10 antibody)
TТ
    Infection
       ( ***paratuberculosis*** , Johne's disease; early-stage
         ***diagnosis*** method for Johne's disease using anti-IL-10
antibody)
    Antibodies and Immunoglobulins
    RL: ARU (Analytical role, unclassified); BSU (Biological study,
    unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL
    (Biological study); USES (Uses)
       (to IL-10; early-stage ***diagnosis*** method for Johne's disease
       using anti-IL-10 antibody)
     ***Interferons***
    RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic
    use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
       (.gamma.; early-stage ***diagnosis*** method for Johne's disease
       using anti-IL-10 antibody)
L11 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
TI
    Peptide T and analogs thereof for the stimulation of cytotoxic T
    lymphocyte (CTL) responses and increasing secretion of ***interferon***
    .gamma, and ***interleukin*** 2, and therapeutic use
    . . . in a subject, comprising administering a CTL activity-stimulating
```

amt. of peptide T or an analog thereof. A method of increasing .gamma .-\*\*\*interferon\*\*\* (IFN-.gamma.) secretion in a subject comprises

AB

```
administering an IFN-.gamma. secretion-increasing amt. of peptide T or an
analog thereof. A method of increasing ***interleukin*** 2 (IL-2)
secretion in a subject comprises administering an IL-2
secretion-increasing amt. of peptide T or an analog thereof. A method of
treating a subject ***diagnosed*** as having a disease assocd, with
reduced CTL activity comprises administering a CTL activity-stimulating
amt. of peptide T or an analog thereof. A method of treating a subject
  ***diagnosed*** as having a disease assocd. with reduced IFN-.gamma.
activity comprises administering an IFN-.gamma. activity-stimulating amt.
of peptide T or an analog thereof. A method of treating a subject
  ***diagnosed*** as having a disease assocd. with reduced IL-2 activity
comprises administering an IL-2 activity-stimulating amt. of peptide T or
peptide T analog cytotoxic T lymphocyte response stimulation;
  ***interferon*** gamma secretion peptide T; ***interleukin*** 2
secretion peptide T
Lymphoma
   (B-cell; peptide T and analogs for stimulation of cytotoxic T
   lymphocyte responses and increasing secretion of ***interferon***
   .gamma. and ***interleukin*** 2, and therapeutic use)
Lymphoma
   (T-cell; peptide T and analogs for stimulation of cytotoxic T
   lymphocyte responses and increasing secretion of ***interferon***
   .gamma. and ***interleukin*** 2, and therapeutic use)
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (TNF-.alpha.; peptide T and analogs for stimulation of cytotoxic T
   lymphocyte responses and increasing secretion of ***interferon***
   .gamma. and ***interleukin*** 2, and therapeutic use)
Carcinoma
   (adenocarcinoma; peptide T and analogs for stimulation of cytotoxic T
   lymphocyte responses and increasing secretion of ***interferon***
   .gamma. and ***interleukin*** 2, and therapeutic use)
AIDS (disease)
   (and AIDS-related lymphoma or sarcoma; peptide T and analogs for
   stimulation of cytotoxic T lymphocyte responses and increasing
   secretion of ***interferon*** .gamma. and ***interleukin*** 2,
   and therapeutic use)
Infection
   (bacterial; peptide T and analogs for stimulation of cytotoxic T
   lymphocyte responses and increasing secretion of ***interferon***
   .gamma. and ***interleukin*** 2, and therapeutic use)
Neoplasm
   (blastoma; peptide T and analogs for stimulation of cytotoxic T
   lymphocyte responses and increasing secretion of ***interferon***
   .gamma. and ***interleukin*** 2, and therapeutic use)
Urogenital system
   (cancer; peptide T and analogs for stimulation of cytotoxic T
   lymphocyte responses and increasing secretion of ***interferon***
   .gamma. and ***interleukin*** 2, and therapeutic use)
Esophagus, neoplasm
Head and Neck, neoplasm
Head and Neck, neoplasm
   (carcinoma; peptide T and analogs for stimulation of cytotoxic T
   lymphocyte responses and increasing secretion of ***interferon***
   .gamma. and ***interleukin*** 2, and therapeutic use)
Uterus, neoplasm
```

ST

TТ

IT

TТ

ΤТ

ΙT

TT

TT

ΙT

```
(cervix, carcinoma; peptide T and analogs for stimulation of cytotoxic
       T lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and
                    ***interleukin*** 2, and therapeutic use)
TT
    Carcinoma
    Uterus, neoplasm
        (cervix; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ΙT
    Intestine, neoplasm
       (colon; peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
IT
    Intestine, neoplasm
        (colorectal; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ΤТ
    T cell (lymphocyte)
        (cytotoxic; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Carcinoma
IT
        (esophageal; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
TТ
    Mycosis
        (fungoides; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and
                    ***interleukin*** 2, and therapeutic use)
ΙT
    Neuroglia, neoplasm
        (glioblastoma; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ΙT
    Carcinoma
    Carcinoma
       (head and neck squamous cell carcinoma; peptide T and analogs for
       stimulation of cytotoxic T lymphocyte responses and increasing
       secretion of ***interferon*** .gamma. and ***interleukin*** 2,
       and therapeutic use)
TТ
    Carcinoma
    Carcinoma
        (head and neck; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ΙT
    Neoplasm
        (histiocytoma; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ΤТ
    Hypoxia
       (hypoxic tumors; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
```

(infection; peptide T and analogs for stimulation of cytotoxic T lymphocyte responses and increasing secretion of \*\*\*interferon\*\*\* .gamma. and \*\*\*interleukin\*\*\* 2, and therapeutic use)

IT Fungi Parasite

TT

Carcinoma

```
(laryngeal squamous cell; peptide T and analogs for stimulation of
       cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
IT Neoplasm
       (metastasis; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
ΤТ
    Skin, neoplasm
       (mycosis fungoides; peptide T and analogs for stimulation of cytotoxic
       T lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Histiocyte
       (neoplasm, histiocytoma; peptide T and analogs for stimulation of
       cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
   Nerve, neoplasm
       (neuroblastoma; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma, and ***interleukin*** 2, and therapeutic use)
    Lymphoma
       (non-Hodgkin's; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
TТ
    Carcinoma
       (oral squamous cell; peptide T and analogs for stimulation of cytotoxic
        T lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Actinobacillus pleuropneumoniae
TT
    Adenoma
    Alternaria alternata
    Anti-AIDS agents
    Antibacterial agents
    Antimalarials
    Antitumor agents
    Antiviral agents
    Aspergillus fumigatus
    Bacillus anthracis
    Bladder, neoplasm
    Blastomyces dermatitidis
    Brain, neoplasm
    Brucella
    Brucella melitensis
    CD8-positive T cell
    Campylobacter
    Candida albicans
    Carcinoma
    Carcinoma
    Chlamydia pneumoniae
    Chlamydia trachomatis
    Chlamydophila psittaci
    Clostridium
    Clostridium tetani
```

Coccidioides immitis

Coronavirus

Coxiella burnetii

Cryptococcus neoformans

Dengue virus

Eastern equine encephalitis virus

Ebola virus Ehrlichia

Ehrlichia ruminantium

Entamoeba histolytica

Escherichia coli

Fungicides

Haemophilus

Haemophilus ducrevi

Haemophilus influenzae

Hantavirus Hematopoietic neoplasm

Hepatitis A virus

Hepatitis B virus

Hepatitis C virus Hepatitis E virus

Hepatitis delta virus

Histoplasma capsulatum

Hodckin's disease

Human

Human T-lymphotropic virus 1

Human adenovirus

Human coxsackievirus

Human immunodeficiency virus

Human immunodeficiency virus 1

Human immunodeficiency virus 2

Human papillomavirus

Human poliovirus

Immunostimulants Influenza A virus

Influenza B virus

Japanese encephalitis virus

Kidney, neoplasm

Lassa virus

Legionella Legionella pneumophila

Leishmania Leishmania major

Leukemia

Listeria ivanovii

Listeria monocytogenes

Liver, neoplasm

Lung, neoplasm

Lymphoma

Mammary gland, neoplasm

Mannheimia haemolytica

Marburg virus

Measles virus

Melanoma Multiple myeloma

Mumps virus

Murray Valley encephalitis virus

Mycobacterium BCG

```
Mycobacterium africanum
Mycobacterium avium
Mycobacterium avium
                     ***paratuberculosis***
Mycobacterium bovis
Mycobacterium intracellulare
Mycobacterium kansasii
Mycobacterium marinum
Mycobacterium tuberculosis
Mycobacterium ulcerans
Mveloid leukemia
Neisseria gonorrhoeae
Neisseria meningitidis
Neoplasm
Nervous system, neoplasm
Neuroglia, neoplasm
Nocardia
Nocardia asteroides
Ovary, neoplasm
Pancreas, neoplasm
Paracoccidioides brasiliensis
Parasiticides
Pasteurella
Pasteurella multocida
Penicillium marneffei
Plasmodium (malarial genus)
Plasmodium falciparum
Plasmodium malariae
Plasmodium vivax
Pneumocystis carinii
Polvomavirus
Prostate gland, neoplasm
Pseudomonas
Pseudomonas aeruginosa
Rabies virus
Respiratory syncytial virus
Rhinovirus
Rickettsia
Rift Valley fever virus
Rotavirus A
Rotavirus B
Rotavirus C
Rous sarcoma virus
Rubella virus
Salmonella
Salmonella typhi
Sarcoma
Schistosoma
Schistosoma mansoni
Shigella
Simian immunodeficiency virus
Sindbis virus
Skin, neoplasm
St. Louis encephalitis virus
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus agalactiae
```

Streptococcus pyogenes

```
Testis, neoplasm
    Toxoplasma gondii
    Trypanosoma brucei
    Trypanosoma cruzi
    Variola virus
    Vesicular stomatitis virus
    Vibrio cholerae
    West Nile virus
    Yellow fever virus
    Yersinia
    Yersinia enterocolitica
    Yersinia pestis
       (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
   Cytokines
        ***Interleukin***
                             ***10***
        ***Interleukin***
        ***Interleukin***
                           12
        ***Interleukin*** 13
        ***Interleukin*** 2
        ***Interleukin*** 4
        ***Interleukin***
                           6
        ***Interleukin***
                            8
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
       (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
    Peptides, biological studies
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
    (Biological study); USES (Uses)
        (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
TТ
    Carcinoma
        (pulmonary squamous cell; peptide T and analogs for stimulation of
       cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
    Neoplasm
       (solid, carcinoma; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    Head and Neck, neoplasm
    Head and Neck, neoplasm
    Larynx, neoplasm
    Lung, neoplasm
    Mouth, neoplasm
       (squamous cell carcinoma; peptide T and analogs for stimulation of
       cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
    Carcinoma
        (squamous cell; peptide T and analogs for stimulation of cytotoxic T
        lymphocyte responses and increasing secretion of ***interferon***
```

```
.gamma. and ***interleukin*** 2, and therapeutic use)
IT Pharynx, neoplasm
       (throat squamous cell carcinoma; peptide T and analogs for stimulation
       of cytotoxic T lymphocyte responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
ΤТ
    Infection
       (viral; peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
          ***interleukin*** 2, and therapeutic use)
      ***Interferons***
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (.gamma.; peptide T and analogs for stimulation of cytotoxic T
       lymphocyte responses and increasing secretion of ***interferon***
       .gamma. and ***interleukin*** 2, and therapeutic use)
    106362-32-7D, C-terminal derivs.
    RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
    use); BIOL (Biological study); USES (Uses)
        (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
    106362-32-7, Peptide T 106362-32-7D, Peptide T, analogs
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
    (Biological study); USES (Uses)
       (peptide T and analogs for stimulation of cytotoxic T lymphocyte
       responses and increasing secretion of ***interferon*** .gamma. and
         ***interleukin*** 2, and therapeutic use)
    107531-09-9 107531-11-3 107531-12-4 107531-14-6 118936-25-7
    118936-26-8 118936-27-9 118936-30-4 118936-31-5 118936-32-6
    118957-86-1 119386-95-7
    RL: PRP (Properties)
        (unclaimed sequence; peptide T and analogs thereof for the stimulation
       of cytotoxic T lymphocyte (CTL) responses and increasing secretion of
         ***interferon*** .gamma. and ***interleukin*** 2, and
therapeutic
       use)
L11 ANSWER 7 OF 7
                    MEDLINE on STN
TI
    Influence of Mycobacterium avium subsp. ***paratuberculosis*** on
    colitis development and specific immune responses during disease.
AB
    . . . and intramural inflammation observed in cases of inflammatory
    bowel diseases (IBD) and veterinary Johne's disease suggests that
    Mycobacterium avium subsp. ***paratuberculosis*** is a causative
    agent. However, an incomplete understanding of the immunological steps
    responsible for the pathologies of IBD makes this conclusion uncertain.
    Sera from ***interleukin*** - ***10*** -deficient (IL-10(-/-)) mice
    with spontaneous colitis displayed significantly higher M. avium subsp.
      ***paratuberculosis*** -specific immunoglobulin G2a antibody responses
    than did sera from similar mice without disease. Pathogen-free IL-10(-/-)
    mice received control vehicle or the vehicle containing heat-killed or
    live M. avium subsp. ***paratuberculosis*** . Mucosal CD4(+) T cells
    from the mice that developed colitis proliferated and secreted higher
    levels of gamma ***interferon*** and tumor necrosis factor alpha after
    ex vivo stimulation with a Vbetall(+) T-cell receptor-restricted peptide
```

CT . . .

from the MPT59 antigen (Ag85B). . .

```
Antigens, Bacterial: IM, immunology
     CD4-Positive T-Lymphocytes: IM, immunology
     Colitis: IM, immunology
     *Colitis: MI, microbiology
     *Colitis: PA, pathology
     Disease Models, Animal
         *** Enzyme-Linked Immunosorbent Assay***
     Humans
      Immunoglobulin G: BL, blood
        *** Interferon Type II: BI, biosynthesis***
         *** Interleukin-10: DF, deficiency***
      Intestinal Mucosa: IM, immunology
     Ligands
     Mice
     Mice, Knockout
         ****Mycobacterium avium subsp. paratuberculosis: IM, immunology***
         ****Paratuberculosis: IM, immunology***
         ****Paratuberculosis: PA, pathology***
      Peptides: IM, immunology
      Receptors, Antigen, T-Cell: IM, immunology
     Receptors, CXCR3
     Receptors, Chemokine: AG, agonists
     Receptors, Chemokine: IM, immunology
    ***130068-27-8 (Interleukin-10)*** ; ***82115-62-6 (Interferon Type***
        II)***
CN. . . 0 (Peptides); 0 (Receptors, Antiqen, T-Cell); 0 (Receptors, CXCR3);
```

0 (Receptors, Chemokine); 0 (Tumor Necrosis Factor-alpha); 0 (antigen 85B,

Mycobacterium \*\*\*paratuberculosis\*\*\* )